# Secretary's Advisory Committee on Genetics, Health, and Society
# Summary of Fourteenth Meeting
# November 19-20, 2007
# Bethesda, Maryland

**Committee Members Present**

Reed Tuckson, M.D., Chair
Mara Aspinall, M.B.A. (appointment pending)
Sylvia Mann Au, M.S., C.G.C.
Paul Billings, M.D., Ph.D., FACP, FACMG
James P. Evans, M.D., Ph.D.
Andrea Ferreira-Gonzalez, Ph.D.
Kevin FitzGerald, S.J., Ph.D., Ph.D.
Julio Licinio, M.D.
Barbara Burns McGrath, R.N., Ph.D.
Paul Steven Miller, J.D. (appointment pending)
Joseph Telfair, Dr.P.H., M.S.W., M.P.H.
Steven Teutsch, M.D., M.P.H.
Marc S. Williams, M.D., FAAP, FACMG
Paul Wise, M.D., M.P.H. (appointment pending)

***Ex Officios*/Alternates Present**

Gurvaneet Randhawa, M.D., M.P.H. (HHS/Agency for Healthcare Research and Quality)
Muin J. Khoury, M.D., Ph.D. (HHS/Centers for Disease Control and Prevention)
Barry M. Straube, M.D. (HHS/Centers for Medicare & Medicaid Services)
Steven Gutman, M.D., M.B.A. (HHS/Food and Drug Administration)
Denise Geolot, Ph.D., R.N., FAAN (HHS/Health Resources and Services Administration)
Francis Collins, M.D., Ph.D. (HHS/National Institutes of Health)
Alan Guttmacher, M.D. (HHS/National Institutes of Health)
Robinsue Frohboese, J.D., Ph.D. (HHS/Office for Civil Rights)
Michael Carome, M.D. (HHS/Office for Human Research Protections)
Inyang Isong, M.D., M.P.H. (HHS/Office on Public Health and Science)
Martin Dannenfelser (Administration for Children and Families)
Michael Amos, Ph.D. (Department of Commerce)
Scott McLean, MC, USA (Department of Defense)
Daniel Wattendorf, Maj, USAF, MC (Department of Defense)
Peter T. Kirchner, M.D. (Department of Energy)
Ellen Fox, M.D. (Department of Veterans Affairs)
Matthew Daynard, J.D. (Federal Trade Commission)

**Executive Secretary**

Sarah Carr, NIH Office of Biotechnology Activities

## NOVEMBER 19, 2007

**Welcome and Opening Remarks**

**Reed V. Tuckson, M.D.**
**SACGHS Chair**

Dr. Reed Tuckson, Chair of the Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS), welcomed those in attendance and stated that the public was made aware of the meeting through notices in the Federal Register and announcements on the SACGHS website and listserv. He encouraged members of the public that wished to address the Committee to register for either of the two public comment sessions. He noted that an extended public comment period was scheduled for the following day to solicit input on the Committee's Draft Report on the Oversight of Genetic Testing. The report was released for public comment on November 5, 2007.

Dr. Tuckson introduced five new SACGHS members appointed by Health and Human Services (HHS) Secretary Michael Leavitt. Mara Aspinall, M.B.A., is president of Genzyme Genetics. She oversees nine laboratories across the United States, as well as operations in Japan that provide worldwide diagnostic testing and genetic counseling services. Ms. Aspinall serves as an *ad hoc* member of the Task Force on Gene Patents and Licensing Practices. Dr. Paul Billings is a consultant at LabCorp who works on special projects with the company's Chief Executive Officer (CEO) and he is an adjunct professor of anthropology at the University of California, Berkeley. He was a member of the joint National Institute of Health (NIH)-Department of Energy (DOE) Task Force on Genetic Information and Insurance and the NIH Recombinant DNA Advisory Committee (RAC). Dr. Paul Miller is the Henry M. Jackson Professor of Law and the Director of the Disability Studies Program at the University of Washington School of Law. He was previously the Commissioner of the Equal Employment Opportunity Commission (EEOC) and, in that capacity, was as an *ex officio* to SACGHS. In addition to providing legal expertise, Dr. Miller will serve the Committee as a consumer representative. Dr. Paul Wise is the Richard Behrman Professor of Child Health and Society at Stanford University. His work focuses on children's health; health outcomes; disparities by race, ethnicity, and socioeconomic status; and the interaction of genetics and the environment. Dr. Rochelle Cooper-Dreyfuss, who was not in attendance due to a prior commitment, is the Pauline Newman Professor of Law at New York University School of Law. She serves as a member of two National Academy of Sciences committees and is the past chair of the American Association of Law Schools Intellectual Property Committee.

Dr. Tuckson welcomed the new members and noted that they were serving in an *ad hoc* capacity pending completion of the appointment process. He welcomed a new *ex officio*, Dr. Inyang Isong, who replaced Dr. Anand Parekh as a representative from the Office on Public Health and Science. Dr. Tuckson announced that *ex officio* Dr. Robinsue Frohboese, the Principal Deputy Director for the Office of Civil Rights, received the Secretary's highest recognition award, the Award for Distinguished Service. Dr. Tuckson congratulated her on behalf of the Committee and commended her dedication in upholding the civil rights of U.S. citizens.

Dr. Tuckson provided an update on the Secretary's Personalized Healthcare Initiative. In September 2007, the Office of the Secretary (OS) issued a report, "Personalized Healthcare Opportunities, Pathways, and Resources," which described HHS activities directed toward the achievement of personalized health care. HHS also released a summary of an expert panel meeting that took place in March 2007, which reported on key stakeholder perspectives and identified five key issues that needed to be addressed to realize the

potential of personalized health care: clinical validity and utility, value and cost effectiveness, the need for data to build evidence and informed clinical decisions, the impact on health disparities, and education of providers and patients. Dr. Tuckson noted that Dr. Andrea Ferreira-Gonzalez, Dr. Steve Teutsch, and Dr. Marc Williams were monitoring the work of the Personalized Healthcare Working Group of the American Health Information Community (AHIC) on behalf of SACGHS.

Dr. Tuckson reviewed the priorities of the Committee and provided an overview of the agenda. Day 1 would focus on a review of the final draft recommendations presented in the pharmacogenomics (PGx) report. The goal was to achieve closure on the recommendations and approve the report for submission to the Secretary of HHS. The morning of Day 2 would be dedicated to a roundtable on genetics education and training of health professionals, led by Dr. Barbara Burns McGrath. On the afternoon of Day 2, Dr. Ferreira-Gonzalez, who was chairing the Task Force on the Oversight of Genetic Testing, would provide a progress report on Task Force activities. Public comments would focus on the draft oversight report. In addition, invited speakers would present an international analysis of methods for regulating oversight.

Executive Secretary Sarah Carr reviewed the Committee's ethical responsibilities. Dr. Tuckson turned the floor over to PGx Task Force Chair Kevin FitzGerald.

## Session on Pharmacogenomics

### *Overview of Final Draft SACGHS Report on Pharmacogenomics and Goals of Session*

**Kevin T. FitzGerald, S.J., Ph.D., Ph.D.**
**Chair, Pharmacogenomics Task Force**

Dr. FitzGerald reviewed the steps taken in the development of the PGx report, including informational sessions, a literature review, interviews with key experts, and a public comment process. Comments were received from the Federal Government, private industry, professional organizations, and individuals. The Task Force modified the report to respond to recurring themes that arose in the comments. The themes indicated the following: the report was overly optimistic about the long-term potential for PGx, more discussion was needed about ongoing international efforts, the Federal Government should encourage collection of DNA samples in clinical trials to facilitate PGx research, criteria were needed to define what PGx information should be included on drug labels, more emphasis should be placed on the need for clinical effectiveness evidence to secure payer reimbursement, a value-based approach for reimbursement of PGx products was needed, and the role of genetic counseling should be further examined.

Each Task Force member reviewed a set of specific comments, and staff members reviewed all comments. Some comments were flagged as requiring discussion by the full Task Force via conference call. Once decisions were made on the disposition of each comment, staff members worked in collaboration with The Lewin Group, a Federal contractor, to revise the report and recommendations.

Dr. FitzGerald reiterated that the goal of the day's session was to finalize the recommendations and vote on their readiness for submission to the Secretary. In December 2007, the Committee would receive the final report via email, after which it would be copyedited, prepared in camera-ready format, and printed. The report was scheduled for transmittal to the Secretary in February 2008, followed by release to the public in March 2008.

Dr. FitzGerald explained that the report was organized into three overarching themes: research and development, gatekeepers, and implementation to improve outcomes in clinical and public health

practice. The report's 15 recommendations included 37 subparts. Dr. FitzGerald explained that as the Committee revised the wording of the recommendations during discussion, staff member Suzanne Goodwin would make corrections in real time and display them on the screen at the front of the room. When all recommendations were revised, the Committee would vote on them collectively.

**Discussion of Final Draft Recommendations**

**Facilitators: Dr. Tuckson and Dr. FitzGerald**

***Research and Development***

The Committee began discussion of the recommendations within the first section of the report, titled "Research and Development." It included subsections on basic research; clinical research; translational research; infrastructure; and ethical, social, and legal issues.

The first part of Recommendation 1, related to basic research, stated, "NIH should put more resources into: 1) basic research on the biochemical pathways associated with drug metabolism and drug action, on the genes and gene variations involved in these pathways, and on functions of those genes related to the safety and effectiveness of drug treatments." Dr. FitzGerald clarified that "more" resources indicated "increased" resources. The group discussed whether these resources should be sought from Congress or by reprioritizing the NIH budget. The following wording was agreed upon for the introductory phrase: "NIH should receive and put more resources into."

Dr. Barry Straube from the Centers for Medicare & Medicaid Services (CMS) commented on the phrase, "safety and effectiveness," which is Food and Drug Administration (FDA) statutory language. He stated that the CMS terms, "medical necessity" and "reasonable and necessary" should be added to the recommendation to lay the groundwork for change in the CMS payment structure. Dr. FitzGerald suggested that this change might be more appropriate in Recommendation 2. Ms. Mara Aspinall proposed changing the wording to "safety and effectiveness of drug treatments and diagnostics" and the Committee agreed.

The second part of Recommendation 1 advocated for more resources for "non-hypothesis-based approaches to the understanding of the relationship between genetic variation and individual's responses to drugs." The Committee made no changes.

Recommendation 2, related to translational research, stated, "As knowledge of the underlying biology accrues, further research will be needed to translate this knowledge into the development of clinically useful PGx tests and technologies and to assess their clinical validity and clinical utility. HHS agencies should facilitate the development of clinically useful PGx technologies by investing more resources into all components of translational research, including the translation of basic research findings into clinical trials, as well as the translation of clinical research findings into clinical and public health practice and policy. One of the emphases of this translational research should be to foster the development of more rapid, cost-effective genotyping technologies." The Committee agreed with Dr. Straube's suggestions to change the wording to "clinical and public health practice, policy, and coverage." They also agreed to delete the last sentence of the recommendation because it was not sufficiently broad.

Recommendation 3 addressed clinical research. Recommendation 3A stated, "Where study results will be used to demonstrate safety and efficacy to support a premarket review application, sponsors and researchers should be encouraged to consult with FDA early in the study design phases. This would help

to ensure that these studies have adequate clinical study design (e.g., sufficient statistical power) and quality controls in place should the research later be submitted for regulatory review." The Committee agreed to Dr. Straube's suggestions to consult with CMS, as well as FDA.

The Committee accepted Recommendation 3B as written: "As appropriate, NIH should consider making FDA's existing quality of evidence standards a component of their assessments of the scientific merits of grant and contract submissions."

Recommendation 3C read, "NIH should encourage grantees and contractors to participate in FDA's Voluntary Genomic Data Submission Program to ensure consistency in data standards that may affect drug prescribing." The Committee modified the recommendation to state that participation in the Data Submission Program should be mandatory in specific situations. The revised recommendation read, "In situations where PGx diagnostics are essential to clinical drug use, HHS should require its grantees and contractors to participate in FDA's Voluntary Genomic Data Submission Program during the exploratory phase of drug development and/or the pre-IDE[1] review process."

Recommendation 3D was added in response to public comments. It read, "HHS should enable the investigation of biomarkers associated with drug response by encouraging sponsors of federally funded clinical drug trials to request appropriate biological samples from research participants." The Committee discussed whether this recommendation was necessary, and if so, whether it should be integrated with another recommendation in a different section of the report. They ultimately agreed to leave it where it was, but developed another sentence to address the need for guidance and standards concerning participant data. They also modified it to parallel a related recommendation in the SACGHS Report on Large Population Studies. The revised recommendation stated, "To enable the investigation of biomarkers associated with drug response, HHS should encourage sponsors of federally funded clinical drug trials to obtain appropriate biological samples from research participants. HHS should develop guidance and standards on how these samples and other participant data will be collected, stored, shared, and used."

Dr. FitzGerald opened discussion on Recommendation 4, which addressed development of PGx products. Recommendation 4A stated, "HHS should ensure that sufficient resources are available to FDA to build on and implement the agency's efforts to develop guidance on the co-development of PGx drugs and diagnostics. FDA's guidance should clarify the review process for co-developed PGx products where the drug is subject to FDA review but the laboratory-developed companion diagnostic test may not be. It also should promote collaboration between drug and diagnostics manufacturers." The Committee revised the wording to read, "FDA should develop and implement guidance on the co-development of PGx drugs and diagnostics. FDA's guidance should clarify the review process for co-developed PGx products. It also should promote collaboration between drug and diagnostics developers."

Recommendation 4B stated, "FDA's Office of Combination Products should coordinate the review of PGx tests and drugs among the various FDA centers/offices to minimize delays in approvals of co-developed PGx products and to ensure timely access to such products." The Committee agreed to delete the phrase "among the various FDA centers and offices" because it was redundant, and they added the word "FDA" prior to the word "review" in the first sentence.

Recommendation 4C read, "HHS should engage all stakeholders in identifying and providing incentives to encourage the development of PGx products, especially for smaller patient populations." Dr. Paul Wise pointed out that some very large patient populations represent small markets, so the Committee changed

[1] Investigational Device Exemptions

the last phrase to, "for smaller patient populations and/or markets." The first sentence was clarified to read, “PGx drugs and diagnostics” instead of “products.”

Recommendation 5, which addressed establishment of an evidence base, had four subparts. Recommendation 5A stated, "HHS should provide resources to identify and address evidence gaps in the analytic validity, clinical validity, clinical utility, and cost effectiveness of PGx. Progress will require high quality data resources, improved methodologies in the design, conduct, and analysis of observational studies, and empirical research on the evidence and standards necessary for making decisions for various purposes (for example, coverage, clinical guidelines, performance metrics) in different clinical contexts."

Dr. Paul Billings stated that the report lacked evidence on the current use of testing. Dr. FitzGerald responded that such data was not available and Dr. Marc Williams agreed, noting that manufacturers vary in terms of their willingness to put their data out for public review. Dr. Teutsch added that the translational process into clinical decision support was being addressed in the Committee’s report on the oversight of genetic testing. After some discussion, the Committee agreed to the following wording for Recommendation 5A, "HHS should identify and address evidence gaps in the analytic validity, clinical validity, clinical utility, and cost effectiveness of PGx. Progress will require high quality data resources; improved methodologies in the design, conduct, and analysis of observational studies; and empirical research on the evidence and standards necessary for making decisions for various purposes (e.g., coverage, clinical guidelines, performance metrics, value-driven health care) in different clinical contexts."

Recommendation 5B read, "HHS should initiate and facilitate collaborations between public (e.g., AHRQ[2], DVA[3], CDC[4], CMS, FDA, NIH) and private entities (e.g., private health insurance plans, pharmacy benefit managers, health care facilities with electronic medical records, clinical research databases, or genetic repositories) to advance the generation and sharing of knowledge on the analytic validity, clinical validity, clinical utility, and cost effectiveness of PGx." Dr. Michael Amos asked that the National Institute of Standards and Technology (NIST) be added to the list of public agencies. Dr. James Evans stated that “value” should be substituted for the term “cost-effectiveness.”

Recommendation 5C stated, "HHS should encourage and facilitate studies on the clinical validity and clinical utility of PGx and the dissemination of study findings, including negative findings where appropriate, through publications, meetings, and an information clearinghouse." The Committee agreed to delete the words “where appropriate,” as they did not add any additional meaning.

Recommendation 5D read, "NIH should provide mechanisms that promote interactions among basic, translational, clinical, and outcomes researchers for the identification of endpoints and data elements to be measured. The goal of these interactions would be to maximize the value and utility of basic and translational research data for downstream assessments of the clinical validity and clinical utility of PGx tests." Dr. Williams suggested substituting “HHS” for "NIH" and the Committee agreed.

Recommendation 6 responded to the need for greater data sharing and database interoperability. Recommendation 6A stated, "HHS should encourage private sector entities (including academic institutions) to share proprietary data voluntarily to advance the development and co-development of PGx

[2] Agency for Healthcare Research and Quality
[3] Department of Veteran’s Affairs
[4] Centers for Disease Control and Prevention

products. Manufacturers should be encouraged to make their data publicly available to allow others to conduct research and publish such studies." The Committee accepted the recommendation as written.

Recommendation 6B stated, "HHS should work with the private sector to identify obstacles to data sharing and to develop solutions to overcome these obstacles (e.g., legal and data confidentiality assurances, intellectual property protections)." Dr. Evans proposed adding “funding of databases” within the parentheses, and Dr. Tuckson added “health information technology" as well.

Recommendation 6C read, "Research, regulatory, and medical records and claims databases need to be interoperable to facilitate research on PGx technologies and to build the necessary evidence base. Interoperability of these databases will facilitate the study of the molecular pathogenesis of disease, the identification of targets for drug development, validation of PGx technologies, assessment of health outcomes associated with the use of PGx technologies, and determination of the cost effectiveness and economic impact of using these technologies.

HHS and other relevant departments (e.g., DVA and DOD[5]) should work with the private sector to improve data sharing and interoperability among databases. Specifically, HHS should work with existing organizations to create uniform genomic data standards, explore ways to harmonize data analysis methodologies, and develop an infrastructure to enable data exchange."

Dr. Ellen Fox remarked that the first sentence overstated the need for interoperable records for the conduct of research. She also suggested that both data sharing and interoperability should be included in the first sentence. She recommended adding text to the report to note that there may be philosophical barriers to interoperability, in addition to the logistical and practical barriers already listed. Dr. FitzGerald asked that the new text be drafted and sent to staff members.

Dr. Gurvaneet Randhawa noted that the first paragraph was very broad in its inclusion of claims databases and medical records databases, but said the second paragraph was very narrow, addressing genomic database standards only. Dr. FitzGerald explained that the Task Force believed it was important to use broad language in the general recommendation, while also emphasizing the need to create uniform genomic data standards. Dr. Randhawa also noted the difference between data sharing and information sharing and asked if both should be included in the recommendation. Dr. FitzGerald stated that the Task Force intentionally focused the recommendation on data sharing.

Mr. Paul Miller noted that Recommendation 6C was formatted differently, as it did not begin with the statement, “HHS should…” Dr. Williams suggested reversing the order of the two paragraphs in the recommendation, so that the format would be parallel with the other recommendations. Dr. Amos suggested adding NIST to the agencies listed, and the Committee discussed changing the wording to clarify that the recommendation was directed to HHS and not to the specific agencies listed. The revised recommendation read as follows:

"HHS should work with other relevant departments (e.g., DVA, DOD, and NIST) and the private sector to improve data sharing and interoperability among databases. Specifically, HHS should work with existing organizations to create uniform genomic data standards, explore ways to harmonize data analysis methodologies, and develop an infrastructure to enable data exchange.

[5] Department of Defense

Data sharing and interoperability of research regulatory medical record and claims databases will facilitate the study of the molecular pathogenesis of disease, the identification of targets for drug development, validation of PGx technologies, assessment of health outcomes associated with the use of PGx technologies, and determination of the cost effectiveness and economic impact of using these technologies."

Recommendation 6D stated, "FDA should identify, initiate, and facilitate research opportunities and public-private partnerships to encourage the development and co-development of PGx products, e.g., through the Critical Path Initiative." Ms. Chira Chen remarked that the wording implied that FDA was paying for the research and asked if that was the case. Dr. Gutman explained that the Critical Path Initiative was being funded through collaborative activities with FDA, including matching funds, and efforts were being made to forge additional partnerships with industry and other Government entities. The Committee decided to add the Biomarkers Consortium as another example of a partnership and accepted the rest of Recommendation 6D as written.

Recommendation 7 addressed personal information protections, stating, "As data access and sharing expand, it will be important to strike the right balance between protecting the privacy and confidentiality of personal data and fostering access to these data for PGx research. Stronger data security measures may be needed as more PGx researchers access patient data." Dr. Joseph Telfair suggested substituting, “will be needed” for “may be needed” and the Committee agreed to move the second sentence prior to the first sentence. Dr. Williams and Dr. Tuckson proposed added a statement recommending that a group such as AHIC's Confidentiality, Privacy, and Security Workgroup be tasked with addressing the issue. The Committee discussed the best way to communicate the need to balance the protection of privacy and confidentiality of personal data with the need to access data for PGx research. Consensus was reached on the following wording for Recommendation 7: "Stronger data security measures will be needed as more PGx researchers access patient data. HHS, through mechanisms such as AHIC's Confidentiality, Privacy, and Security Workgroup, should develop guidance on how to balance the protection of privacy and confidentiality of personal data with access to these data for PGx research."

Recommendation 8 addressed population stratification in drug response. Recommendation 8A stated, "Because genomic factors may be more meaningful predictors of drug response than race and ethnicity categories, FDA should develop guidance that encourages the collection and analysis of genetic and other biological factors that may better explain differences in drug response." The Committee made the wording more precise to ensure that it was not subject to misinterpretation. The revised recommendation read, "FDA should develop guidance that encourages the collection and analysis of genetic and other biological factors that may be better biological predictors of individual differences in drug response than broad categories such as race, ethnicity, and gender."

Recommendation 8B read, "When drugs are shown to be effective in certain racial and ethnic subpopulations (e.g., BiDil), FDA should encourage manufacturers to conduct additional postmarket studies to identify biological, social, behavioral, and environmental markers that may underlie the differential drug response." The Committee agreed to add “genetic” to the recommendation to parallel the language in Recommendation 8A, and they decided that not enough was known about BiDil to include it as an example. The revised Recommendation 8B read, "When drugs are shown to be more effective in certain racial and ethnic subpopulations, FDA should encourage manufacturers to conduct additional postmarket studies to identify genetic and other biological, social, behavioral, and environmental markers that may underlie the differential drug effects."

The discussion of recommendations related to Research and Development concluded.

***Gatekeepers***

Dr. FitzGerald introduced the recommendation concerning “Gatekeepers,” i.e., industry; FDA, CMS and other third-party payers; and clinical practice guideline developers. He explained that these entities can enable, halt, or redirect the course of PGx technologies and affect integration and patient access. Dr. Ferreira-Gonzalez suggested adding text to the report to further clarify the CMS role in regulating laboratories through the Clinical Laboratory Improvement Amendments (CLIA). She agreed to draft and submit her comments to staff.

Recommendation 9 addressed reimbursement of PGx products, stating, "In clinical situations where a PGx test has been shown to enhance safety and/or effectiveness of clinical management (i.e., has demonstrated clinical utility compared to alternative management strategies) and provides value comparable to or an improvement over other covered services, public and private health plans should provide coverage and reimbursement for the test and the most clinically appropriate drug as indicated by PGx test results." Dr. Williams commented that this recommendation went beyond the scope of authority of the HHS Secretary and should not reference private health plans. He also stated that the recommendation should ask the Secretary for clarification from CMS on whether PGx testing will be considered a preventive service and receive coverage. Staff member Suzanne Goodwin noted that a similar recommendation had been made to the Secretary in the Committee’s coverage and reimbursement report, and the PGx Task Force had decided not to reiterate it. Dr. Williams maintained that it should be included.

Dr. Straube agreed with Dr. Williams and stated that CMS is governed by statute in terms of coverage decisions. Prior to 1995, safety and effectiveness (as determined by FDA) was the standard for coverage. However, that was no longer the case and CMS was struggling to define the meaning of "reasonable and necessary." Dr. Straube added that the concept of “value” is not used by CMS in making coverage decisions. Dr. Williams suggested that Recommendation 9 ask the Secretary to explore with CMS the issue of whether PGx tests will be excluded from coverage based on screening or prevention language and whether there are non-statutory solutions that would allow consideration of coverage under the usual CMS mechanisms.

Dr. Straube suggested recommending that the Secretary ask CMS to produce a guidance document on the current status of genetic testing as it relates to PGx, and include data obtained from a survey of the private sector. The survey would help identify coverage policies in the private sector so that CMS could compare them to restrictions under Medicare and try to align their policies. Once this data was analyzed, CMS could make recommendations to the Secretary on available options. Dr. Fox suggested surveying public as well as private health care plans. Dr. Wise remarked that Medicaid and the State Children’s Health Insurance Program (SCHIP) should be included in the recommendation. The revised version of Recommendation 9 read, “CMS should develop a guidance document detailing current Medicare, Medicaid, and State Children’s Health Insurance Program coverage and reimbursement of PGx products. CMS also should survey public and private health plans about their decisionmaking processes and coverage policies to help inform its future PGx coverage and reimbursement decisions.”

Ms. Sylvia Au suggested that a new recommendation be developed to acknowledge the importance of the prior recommendations sent to the Secretary on issues of coverage and reimbursement. The Committee agreed to add Recommendation 9B, “Because the issues identified in the SACGHS coverage and reimbursement report are relevant to issues in this report, SACGHS urges HHS to act on the coverage and reimbursement report’s recommendations.”

The Committee concluded discussion on Recommendation 9, the only recommendation concerning Gatekeepers.

***Implementation of PGx to Improve Outcomes in Clinical and Public Health Practice***

Dr. FitzGerald introduced discussion of the recommendations on PGx implementation. They addressed the following issues: education and guidance; information technology; economic implications of PGx; ethical, legal, and social issues in clinical implementation of PGx; and coordination of HHS's PGx activities.

Recommendation 10 consisted of eight subparts. Recommendation 10A stated, "HHS should assist State and other Federal agencies and private sector organizations in the development, cataloguing, and dissemination of case studies and practice models relating to the use of PGx technologies." The Committee accepted the recommendation as written.

Recommendation 10B addressed the use of PGx technologies in clinical practice and public health practice. It read, "HHS should assist professional organizations in their efforts to help their memberships achieve established competencies on the appropriate use of PGx technologies. HHS also should encourage and facilitate collaborations between the organizations and the Federal Government around these activities." As the Committee agreed that there were few, if any, established competencies, the "word "established" was deleted. The Committee also changed the word "memberships" to "members" and accepted the remaining text of the recommendation.

Recommendation 10C stated, "As evidence of the clinical validity and clinical utility for a PGx technology accrues, HHS should support the conduct of systematic reviews and technology assessments to summarize the evidence base. These systematic reviews and technology assessments should be disseminated to professional organizations to facilitate the development of clinical practice guidelines." Dr. Williams suggested deleting the words "professional organizations," because many types of organizations would be developing clinical practice guidelines. The Committee agreed and accepted the recommendation with no further changes.

Recommendation 10D read, "HHS should facilitate the development of evidence-based clinical practice guidelines and dosing guidelines by supporting consensus-building efforts among guideline developers. These consensus-building efforts should include development of standards that define the minimum levels of evidence required to support guideline decisions. These standards should take into account the clinical contexts (e.g., prevention, diagnosis, treatment) in which the PGx test may be offered. Consensus-building efforts also should include standardization of guideline development methods." The Committee agreed to delete the last sentence because a standardized process was already established at the website, Guidelines.gov. They accepted the rest of the recommendation as written.

Recommendation 10E was developed in response to public comments. It stated, "To inform the development of PGx tests and dosing guidelines, HHS should fund clinical trials that provide evidence on whether PGx information is clinically useful and, if so, how to use this information in addition to other relevant factors (e.g., gender and age of patient, other medications being taken)." Dr. Randhawa noted that "trials" should be changed to "studies." The Committee agreed with Dr. Evans suggestion that the last clause, "…and, if so, how to use this information, in addition to other relevant factors…" should be deleted, because this concept had already been addressed. The revised Recommendation 10E stated, "To inform the development of PGx tests and dosing guidelines, HHS should fund clinical studies that provide evidence on whether PGx information is clinically useful."

Recommendation 10F read, "Professional organizations are encouraged to submit clinical practice guidelines that they develop for PGx testing to AHRQ's National Guideline Clearinghouse to facilitate dissemination and encourage their implementation and use." The Committee decided to introduce the recommendation by stating, "The Secretary should encourage organizations to submit…" and accepted the rest of the text as written.

Recommendation 10G stated, "FDA and drug manufacturers should focus more attention on ensuring that all relevant PGx information is included in drug labels in a timely manner. When a PGx test is mentioned in a drug label, information should be included about the test's analytical validity, clinical validity, clinical utility, dosing, adverse events, or drug selection for clinicians to use when making treatment decisions based on PGx test results. FDA should provide guidance on the standards of evidence that must be met for PGx information to be included in the label." The Committee refined the wording of the first sentence of Recommendation 10G to read, "FDA should work with manufacturers to ensure that all relevant PGx information is included in drug labels in a timely manner." They accepted the rest of the text as written.

Recommendation 10H addressed dissemination, stating, "NIH and FDA should continue expanding the Internet-based DailyMed project, which provides up-to-date, real-time prescription drug label package insert information to people with Internet access. To ensure that all sectors of the public have access to this information, FDA and NIH should develop other ways to disseminate this information." The Committee accepted the recommendation as written.

Recommendation 11 addressed public education and engagement. Recommendation 11A stated, "To inform the public about the availability, benefits, risks, and limitations of PGx technologies, HHS should ensure that credible educational resources are widely available through Federal websites and other appropriate media." The Committee agreed to delete the words "credible" and "appropriate," as HHS has internal standards for ensuring the quality and appropriateness of the resources it disseminates. The rest of the recommendation was accepted without changes.

Recommendation 11B read, "HHS should use existing public consultation mechanisms to engage the public in a constructive dialogue regarding the potential benefits, risks, and limitations of PGx technologies. This dialogue should include an assessment of their perceptions of and receptiveness to PGx and their willingness to participate in clinical research studies involving these technologies." The Committee made several editorial changes to Recommendation 11B, as follows, "HHS should use existing public consultation mechanisms to dialogue on the potential benefits, risks, and limitations of PGx technologies. This dialogue should include an assessment of their perceptions of and receptiveness to PGx and their willingness to use these technologies and participate in studies."

Recommendation 12 addressed health information technology. Recommendation 12A stated, "The Office of the National Coordinator for Health Information Technology, through the activities of the American Health Information Community, and in consultation with DVA and DOD, should take steps to ensure the inclusion of clinically validated PGx test results into patient records, along with decision support systems and tools to enhance appropriate test use and interpretation. Decision support systems and tools should include information about the availability of PGx tests, patient test results, and relevant information for making treatment and dosing decisions.

"As the infrastructure develops, HHS should account for the needs of basic clinical and translational researchers to ensure that secure, consented clinical outcomes information is available to accelerate integration of PGx breakthroughs into clinical practice.

"HHS should support efforts to establish standards for the development of electronic clinical decision support systems and tools. PGx test clinical practice guidelines should be developed in a manner that allows for their integration into such systems and tools."

Dr. Williams noted that the role of AHIC was to develop platforms for electronic health records, not to address the content of the records in any way. He stated that the key point of Recommendation 10 should be to help ensure that new developments in health information technology support the inclusion of genomic information. Dr. Tuckson added that the last sentence in the first paragraph and the entire second and third paragraphs were redundant and should be deleted. To address the issue of content, Dr. Randhawa and Dr. Williams recommended that pilot studies be undertaken by the knowledge generation agencies of HHS. They suggested that these agencies examine the impact of clinical decision support systems for PGx technologies on clinical practice at the point of care to maximize evidence-based best practices. Dr. Tuckson and Dr. Straube cautioned that Government funding would likely not be available to conduct such studies. The wording of the recommendation was changed to reflect the idea that pilot studies could be either publicly or privately funded. The Committee agreed on the following revised version of Recommendation 12A:

“The Office of the National Coordinator for Health Information Technology, through the activities of the American Health Information Community, should study how clinically validated PGx test results are being incorporated into electronic health records. HHS, in consultation with DVA and DOD, also should take steps to ensure that the necessary infrastructure is in place to support the representation of PGx data in electronic health records for use in decision support systems and tools. HHS should explore the development of pilot studies that examine the impact of clinical decision support systems for PGx technologies on clinical practice at the point of care to maximize evidence-based best practices.”

Recommendation 12B read, "Until electronic health record systems become a universal feature of the health care system, HHS should identify other ways to make best clinical practices for PGx more readily available to help providers as they are developed." Dr. Evans stated that Recommendation 12B was redundant with previous recommendations, and the Committee agreed to delete it.

Recommendation 13 addressed the economic implications of PGx, stating, "To ensure that investments in PGx are well spent, HHS should gather data to assess the economic value of investments in PGx relative to other health-related investments. This assessment should encompass the cost-effectiveness of PGx technologies and take into account their short- and long-term impacts on specific sectors in society as a whole."

Ms. Sylvia Au and Dr. Tuckson stated that it was unrealistic to ask for Federal funding to assess the economic value of PGx, and Dr. Tuckson suggested deleting the recommendation. Dr. Teutsch and Dr. Fox advocated for keeping it, because of the tremendous potential of PGx to reduce other health care expenditures. Dr. Straube supported deletion of the recommendation, stating that those who have a business interest in these technologies will make the case for their use. Dr. Telfair suggested that the intent of the recommendation (i.e., assessing cost-effectiveness) be incorporated into the other recommendations that addressed studies on PGx. The Committee indicated by a show of hands that they agreed with Dr. Telfair’s suggestion. They agreed that Recommendation 5A could be interpreted to include the proposal in Recommendation 13. New text would be added to the report to make this point more explicit.

Recommendation 14 addressed the ethical, legal, and social implications of PGx research, stating, "NIH, in collaboration with other agencies, should continue to encourage and fund research on the ethical, legal,

and social implications of PGx. This research should include studies of whether integration of PGx into clinical and public health practice exacerbates health and health care disparities, limits access to or decreases the quality of health care, increases medical liability, or results in genetic discrimination." Dr. Billings and Dr. Wise asked if the Committee could make a stronger commitment to the reduction and prevention of health care disparities by asking the Secretary to address relevant policy issues. During further discussion, Dr. Williams and Dr. Teutsch noted that it was important to focus the recommendation only on those health care disparities related to PGx. The revised recommendation stated, "HHS should support policies that afford access to PGx technologies in ways that reduce health and health care disparities, improve quality of health care, and prevent genetic discrimination. To this end, HHS should continue to encourage and fund research in support of this goal."

Recommendation 15 dealt with the coordination of PGx activities and was in part added at the request of SACGHS *ex officios*. Recommendation 15A stated, "An interdepartmental workgroup should be established to review these recommendations, assess whether and how to implement them, monitor HHS progress, and report back to SACGHS. The workgroup also could serve as a forum for discussion of other PGx activities." Dr. Williams suggested that the workgroup prioritize the recommendations. Other Committee members suggested that the Secretary make the decision on how to follow up on the recommendations, and they made several editorial changes, which resulted in the following wording, "The Secretary is requested to take all necessary steps to review and prioritize these recommendations, assess whether and how to implement them, monitor HHS's progress, and report back to SACGHS."

Recommendation 15B stated, "HHS should assess the level and adequacy of resources being devoted to support the integration of PGx into clinical and public health practice to be sure that gaps and opportunities identified in this report are addressed." The Committee agreed that the content of this recommendation was already included in 15A and they deleted it.

Dr. Tuckson opened the floor for public comments, with further discussion of the PGx recommendations to follow.

**Public Comments**

Mr. Robert Reinhard submitted comments via email.

**Robert Reinhard**
**Community Advisory Group, San Francisco Department of Public Health Research**

Dr. Reinhard noted that during the discussion of PGx recommendations, Dr. FitzGerald questioned whether sufficient evidence of a genuine pharmacogenetics-based effect in drug development had yet been demonstrated. Dr. Reinhard said that in the area of HIV drug research, the answer was yes. A peer-reviewed study described ways to reduce central nervous system effects associated with the administration of Sustiva based on genetic differences in the patient population. In his earlier written comments, dated May 17, 2007, Dr. Reinhard described the important genetic test component necessary in the prescribing of other HIV drugs. He said these examples illustrated the importance of this form of personalized medicine and the importance of facilitating co-development of diagnostics and drug development for the benefit of patient care for serious life-threatening illnesses.

**Amy Miller**
**Public Policy Director**
**Personalized Medicine Coalition**

Amy Miller represented the Personalized Medicine Coalition (PMC), a federation of over 100 organizations from a broad spectrum of academic, industrial, patient, provider, and payer communities that seek to advance the understanding and adoption of personalized medicine concepts and products for the benefits of patients. She reiterated the public comments she made during the previous SACGHS meeting concerning business incentives for personalized medicine. She stated that: 1) Federal funds should be appropriated to expand and accelerate genetic and genomic research through research and development grants; 2) FDA should put in place an accelerated approval process for personalized therapeutics and diagnostics developed together or developed separately, but designed to work together; 3) Reimbursement practices governing new technologies have a profound impact on both patient access and the incentives of industry to develop new technologies. Therefore, PMC urged SACGHS to suggest new policies that expand payer coverage and reimbursement of personalized medicine products and services focused on disease prevention and that improve the efficiency and value of the health care system. She noted that PMC is developing ideas on reimbursement models that will promote personalized medicine and PGx. They planned to articulate these ideas through white papers, workgroups, and public meetings.

Ms. Aspinall asked Ms. Miller if she believed the PGx recommendations fully addressed reimbursement issues. Ms. Miller stated that the recommendation that prevention be covered by CMS was valuable, but as a beginning step only. She was not sure the recommendations fully articulated the reimbursement issue, which was, in part, why PMC planned to dedicate considerable time and effort to more fully articulating the ways that reimbursement can drive the adoption of personalized medicine.

Dr. Tuckson thanked those who provided comments and turned the floor back to Dr. FitzGerald.

**Reaching Consensus on Final Draft Recommendations and Draft Report**

**Kevin T. FitzGerald, S.J., Ph.D., Ph.D.**
**Chair, Pharmacogenomics Task Force**

Dr. FitzGerald read the text of each of the revised recommendations so that the Committee could suggest final changes and vote on approving the PGx report and recommendations. Dr. Williams proposed a change to Recommendation 9B, "As the issues identified in the SACGHS Coverage and Reimbursement Report are still current, SACGHS urges HHS to act on the report's recommendations." He suggested changing “still current” to “are relevant to recommendations in this report”. The Committee approved the change. Dr. Tuckson then led the Committee in a vote that unanimously approved the full report and recommendations. Dr. FitzGerald thanked all those who worked on the report. Dr. Tuckson adjourned Day 1 of the meeting.

# NOVEMBER 20, 2007

**Welcome and Opening Remarks**

**Reed V. Tuckson, M.D.**
**SACGHS Chair**

Dr. Tuckson introduced the roundtable session on the education and training of health professionals, asking members to listen carefully and query the experts who were presenting. He turned the floor over to Dr. Burns McGrath for an overview of the session.

**Roundtable on Genetics Education and Training of Health Professionals**

**Overview of Session**
**Barbara Burns McGrath, R.N., Ph.D.**
**Research Associate Professor**
**University of Washington School of Nursing**

Dr. Burns McGrath said the Committee was addressing the topic of genetics education in a roundtable format, as it had done several years previously. The need to explore issues around education and training had been part of the SACGHS strategic plan since its inception, and in 2003, a similar roundtable resulted in a resolution presented to the Secretary of HHS in 2004. The resolution urged the Secretary to take action in the following areas:

- Incorporate in HHS programs and policies the philosophy that genetic information is an integral part of all health care; facilitate integration by collaborating with State, Federal, and private organizations.
- Promote and support initiatives that integrate genetics and genomics in education and training of health professionals. This point included the promotion of family history information, supported point-of-care models, and linked to the Health Information Technology (HIT) initiative.
- Encourage and support programs that promote diversity and cultural competency of the health care work force. This included issues associated with disability rights.
- Work with relevant organizations to incorporate knowledge of genetics and genomics in accreditation, licensure, and certification processes. It suggested using the accreditation process as a driver for educational programs.
- Support Federal programs for faculty training and clinical application-based education models, particularly those that include ethical, legal, and social issues.
- Promote consumer education and support K-12 education programs. The K-12 issue was intended to establish a pipeline for a future diverse work force.

Dr. Burns McGrath noted that changes since 2004 indicated that it was time for the Committee to take another look at the issue. She stated that the roundtable to follow would include the perspectives of key people with knowledge of professional development. The disciplines represented included medicine, nursing, genetic counseling, physician assistants, public health, education, and laboratory medicine. The topics identified as part of the day's discussion included professional education and training programs; progress on a diverse work force; emerging issues in the field, in particular, complex gene-environment interactions; identifying emerging stakeholders; and genetic family history. Dr. Burns McGrath asked the

Committee to consider two questions as they listened to the speakers: Does the topic of genetic education and training continue to be an area of concern consistent with the SACGHS charter? If so, what elements are most important to address? She began the roundtable with the introduction of Mr. Joe McInerney.

**Overview of Education Initiatives for Health Professionals**
**Joseph McInerney, M.A., M.S.**
**Executive Director**
**National Coalition for Health Professional Education in Genetics**

Mr. McInerney, Director of the National Coalition for Health Professional Education in Genetics (NCHPEG), said the organization addresses genetics education for health professionals on a full-time basis. He asked the Committee to consider how much genetics knowledge primary care physicians should have, and whether they should be able to diagnose, treat, and counsel about genetic diseases. He stated that a primary care physician should have enough knowledge to recognize a problem as genetic and enough familiarity with genetic principles to be able to use the literature wisely or consult with a geneticist.

Some of the major challenges NCHPEG encounters as they try to bring genetics education into curricula for health professionals include: crowded curriculum, misconceptions about genetics, a lack of knowledgeable faculty, a disconnect between basic science and clinical experiences during training, failure to integrate genetics across the curriculum, and inadequate representation of genetics on certifying exams. Challenges to the integration of genetics into primary care include: a dearth of genetics professionals, lack of knowledge and misconceptions about genetics among primary care providers, inadequate family histories, and a lack of clinical guidelines related to genetics. Mr. McInerney stated that health professionals often ask what they should do differently; they want concrete steps that will improve outcomes for their patients. Although genetics information has intrinsic value, primary care providers are often not interested in it unless there are practical and reimbursable health care options.

Mr. McInerney reviewed some data on whether medical schools have fully incorporated genetics and genomics into their curricula. A May 2007 paper in *Academic Medicine* described a survey of 149 U.S. and Canadian medical course directors. Seventy-seven percent reported that they teach medical genetics in the first year. Only 47 percent said they incorporated genetics in the third or fourth year, indicating that there is a separation of genetics from basic science and during the clinical years. Eighty-six percent said they cover general genetics concepts, but only 11 percent said they address practical applications of genetics. Forty-six percent reported offering a standalone course and 54 percent said they integrate medical genetics into another course. An analysis conducted by NCHPEG and the Genetic Alliance indicated that consumers did not give their providers high evaluations on understanding genetics.

The central questions and challenges in education and training of health professionals include: What content is appropriate and for whom? Which clinical behaviors and attitudes should change? How can educational programs get to the people that need them and how can we ensure that they are used? How do we define and measure success?

Mr. McInerney stated that NCHPEG recently produced a third edition of their publication, *Core Competencies in Genetics.* He described a NCHPEG program that was attempting to provide access to genetics content in a clinically relevant way, known as GeneFacts. It was developed because open-source genetics databases often present reliable content, but in a way that is inappropriate for physicians, while subscription databases present content that is easily accessible, but not always accurate. GeneFacts

attempts to find a middle ground, offering a point-of-care decision support system with clinically relevant and genetically sound material written by primary care providers and geneticists.

Mr. McInerney concluded by stating that the terms “genetic disease” and “non-genetic disease” create barriers in communicating with health care professionals. He said the question to consider is the role genetic variation is playing in the onset and expression of disease in a particular person.

**Question-and-Answer Session**

Dr. Khoury asked whether NCHPEG used the concept of evidence-based medicine when working with primary care providers to help determine which methods of diagnosis and treatment need to move into mainstream medicine. Mr. McInerney said they had not addressed the concept of evidence-based medicine as carefully as they should in some programs. However, they work with the provider community to identify the cases and clinical settings that are most relevant. They also work closely with the Genetic Alliance on a CDC-funded project called Access to Credible Genetics Information. This program applies the principles of evidence-based medicine to the selection of genetics information that providers and patients can use to make informed decisions to improve health care.

## Presentation of Certificates

Dr. Tuckson stated that he was pleased to honor three outstanding members of SACGHS who had rotated off the Committee. Cindy Berry was an attorney at Powell Goldstein, specializing in health care law, medical malpractice defense, and commercial litigation. She was previously a member of the Secretary's Advisory Committee on Genetic Testing (SACGT). Dr. Tuckson presented her with a certificate of appreciation from the Secretary. Dr. Tuckson asked Ms. Chira Chen to come forward. Ms. Chen was a representative of the San Francisco Advocacy Corps, a volunteer group that shares the patient's perspective with breast cancer researchers at the University of California. She served as a reviewer for breast cancer research grant applications for the Department of Defense and was a staff research associate at the University of California San Francisco Comprehensive Cancer Center. Dr. Tuckson presented her with a certificate of appreciation from the Secretary. Dr. Tuckson then presented Dr. Hunt Willard with a certificate from the Secretary expressing appreciation for his expertise in human genetics and genomics and his leadership on SACGHS issues. Dr. Tuckson invited the three former members to remain and take part in the Committee’s deliberations.

The Committee returned to the education and training roundtable. Dr. Burns McGrath introduced Dr. Norman Kahn.

## Roundtable on Genetics Education and Training of Health Professionals, Cont’d

**Progress in Integrating Genetics into Primary Care**
**Norman Kahn, Jr., M.D.**
**Vice President for Science and Education**
**American Academy of Family Physicians**

Dr. Norman Kahn represented the perspective of medical education at the American Academy of Family Physicians (AAFP). He described a project called Genetics in Primary Care (GPC), which began in 1998 and received funding from NIH, the Health Resources and Services Administration (HRSA), and AHRQ. Its goal was to educate medical faculty about genetics so they could incorporate it into medical education at undergraduate and graduate levels. They brought together the primary care community (e.g., family

medicine, pediatrics, internal medicine) and the genetics community (e.g., medical genetics, genetics counselors, the Genetic Alliance), and discovered that there were two different languages, cultures, and perspectives. The primary care community needed to learn to look through a genetics lens to expand differential diagnosis to include genetic conditions; use family history to identify genetic conditions; provide non-directive counseling; and recognize the ethical, legal, and social issues raised by a genetic diagnosis. The genetics community needed to learn to see genetics through a primary care lens to evaluate the utility of genetic information in terms of health outcomes, respect for patient preferences, and the potential for use in longitudinal care.

Nineteen faculty teams at different medical schools participated in GPC. The curriculum included seven topics that have a genetic component: breast cancer, cardiovascular disease, colorectal cancer, congenital hearing loss, dementia, developmental delay, and hemochromatosis. The primary care community would not generally consider most of these genetic disorders. However, learning to think genetically allowed doctors to recognize the importance of the family history component, distinguish among different types of cancer, and determine which disorders are genetic and which are not. Several complementary tools and resources were used in the program. These included a "Genetics 101" curriculum, aids to family history-taking in primary care, "red flags" to alert primary care doctors to potential genetic bases for disease, evidence-based medicine tools for interpreting genetic tests, and cultural competency information relevant to advances in genetics.

Having focused on undergraduate and graduate medical education, AAFP decided to focus on practicing clinicians after 2003. They created a program called Annual Clinical Focus (ACF) and spent the year of 2005 focusing on genomics and educating primary care clinicians at the practice level. The topics included family history, breast cancer, Alzheimer's disease, colorectal cancer, bipolar disorder, newborn screening, hemochromatosis, and autism. Dr. Kahn presented a video created by the program that featured a family physician modeling interaction with a patient. Other videos developed by the program featured a nurse practitioner, a physician assistant, and a pediatrician. The program relied primarily on Web-based delivery, and as of November 2007, 30,000 unique visitors had come to their website. This led them to believe that the program was a very good vehicle for educating clinicians in practice.

Dr. Kahn concluded by stating that a tremendous amount of work was still needed to teach primary care clinicians to look through a genetics lens. He noted that there are only 2,000 certified medical geneticists and 2,000 genetic counselors in the United States, meaning that many communities lack these professionals. Therefore, primary care clinicians must be comfortable interpreting and following up on genetic tests with patients and families.

**Question-and-Answer Session**

Dr. Tuckson asked if there was an effort to coordinate the program with certifying boards. Dr. Kahn said more work was needed in that area. Dr. Williams noted that some formal work on board certification and genetics would be published in the near future based on research by Darrell Waggoner from the University of Chicago.

Dr. Burns McGrath introduced Beth Pestka from the International Society of Nurses and Genetics (ISONG).

**Nursing Competencies and Genetics Training**
**Elizabeth Pestka, M.S.**
**Assistant Professor of Nursing**
**Mayo Clinic College of Medicine**

Ms. Beth Pestka represented the Mayo Clinic in Rochester, Minnesota, which has an exemplary model of genomics education for nurses. She stated that prior to 2004, there were many genetics initiatives in the profession of nursing, but they were not well planned. In 2005, Dr. Jean Jenkins and Ms. Cathy Calzone of ISONG headed a group with the goal of creating a concentrated and cohesive plan for integrating genetics and genomics into nursing. They began contacting the 80 recognized nursing organizations in the United States and garnered support from 48 of those organizations. In a 2005 meeting, consensus was reached on a set of essential nursing competencies. In 2006, another meeting was held to identify an integration plan for implementing these competencies into education and practice. The implementation plan had three areas of focus: academic nursing, practicing nurses, and regulatory and quality control; each had specific goals to be achieved within 5 years.

Ms. Pestka discussed practicing nurses based on her extensive experience at the Mayo Clinic. She explained that the Mayo Clinic's implementation plan was based on Everett Rogers' Diffusion of Innovations theory. According to this theory, the knowledge stage occurs first, which in this case was educating nurses in genomics. The second stage, persuasion, addressed the question, Why is genomics important or relevant for me? Information and examples were used to communicate this information. Decision making was the third stage, i.e., Is genomics worth the effort? Next was the implementation stage: How do I include genomics in my practice? The last stage was confirmation: Am I competent in utilizing genomics in my practice?

Ms. Pestka played a video clip of a patient expressing his hopes for the success of pharmacogenomics for himself and his family members. The Mayo Clinic created a series of similar video clips related to various diagnoses, and they were found to be very helpful in nursing education efforts.

The president and CEO of the Mayo Clinic, Dr. Denis Cortese, once stated that the future of health care lies in translating genomics advances into practice. Patients will go to the providers that are best informed and best equipped to provide genomics services. The Mayo Clinic therefore established a center for individualized medicine based on genomics information and they received the Magnet Prize for their nursing genomics program. This award has been described as the Nobel Prize of nursing. The award-winning program began in 2001, and was developed incrementally. Presentations were given to leadership groups, and program leaders wrote articles and started a nursing staff development curriculum, which consisted of a 4-hour class. Posters were displayed at nurses' fairs to gain visibility for the effort. There is an intranet specific to nursing at the Mayo Clinic, which was being increasingly utilized. The group sponsors about 12 conferences annually, most of which include genetics and genomics. When nurses go into specialty areas, such as hematology, oncology, or psychiatry, they receive additional training in genomics.

Ms. Pestka said the centerpiece of the program was the nursing genomics interest group. Anyone with an interest could join this grassroots group, which was focused on peers teaching peers. Once an individual was educated in the competencies and was teaching peers, they would be asked to role model the competencies. This could take many forms, such as displays of information on bulletin boards or the creation of binders of articles.

Ms. Pestka stated that the list of competencies was too general, so they built on the basic competencies and applied them to the nursing process. They developed an assessment process that included data collection on family history, family pedigree, environmental factors, physical findings, and patients' knowledge and questions. This information assisted in the planning process. The actual interventions included patient education; discussing family risks and preventative measures; testing; treatment; pharmacogenomics; ethical, legal, social, and cultural issues; and support services. She noted that a genetics referral would be made if indicated. Finally, the services provided were evaluated. This model was accepted for publication in the *American Journal of Nursing*.

Ms. Pestka described barriers to the training of nurses in genomics, including: time for education, time to implement in practice, time to evaluate competency, a lack of education resources, and no centralized location for resources for nurses. She closed by stating that genetics and genomics represent the future for all professions in health care.

**Question-and-Answer Session**

Dr. Licino noted that the patient in the video clip had unrealistic expectations about the way genomics might help cure his psychiatric disorder. Ms. Pestka replied that part of the education process consists of reframing patient expectations in realistic terms.

Ms. Aspinall asked if a measurement tool had been developed to look at the progress of the program and monitor how much information was being internalized by the nurses. Ms. Pestka said they conducted one survey that took place at a psychiatric nursing conference, and it indicated significant learning on the part of the nurses. She explained that their focus was on the competency aspect, i.e., Will the nurse be able to apply this in practice? Ms. Aspinall asked if competency was being measured and Ms. Pestka said they conducted one pilot study related to hematology and oncology nurses and they were working to replicate the study in other settings. The measurement approach used was self-report.

Dr. Burns McGrath thanked Ms. Pestka and introduced Dr. Melissa Fries from the American Academy of Medical Genetics (ACMG).

**Role of Professional Societies**
**Melissa Fries, M.D.**
**Director of Genetics and Fetal Medicine**
**Washington Hospital Center**

Dr. Melissa Fries addressed the Committee as both a practicing medical geneticist and as the Chair of the Education Committee for the American College of Medical Genetics (ACMG). She stated that education requirements for a medical geneticist consist of a 2-year residency program, for which there are 48 Accreditation Council for Graduate Medical Education (ACGME)-accredited programs in medical genetics. Some institutions require a 3-year program. There is a prerequisite of 2 prior years of initial residency training, such as in pediatrics or internal medicine. There are also 5-year combined pediatrics and genetics programs and internal medicine and genetics programs. Several fellowship programs are available, such as in maternal/fetal medicine and genetics (a 4-year fellowship), and a molecular-genetic pathology program (a 1-year fellowship). These residencies can only be entered after medical school.

Dr. Fries noted that there were 196 medical genetics residency positions, with only 47 percent filled. By comparison, 93 percent of available positions in family practice were filled. Although the programs were in place, they were not being chosen by medical students. If this trend were to continue, there would be a

declining number of people available to meet the need for genetics professionals. This concern was the subject of considerable research. In 2005, The Banbury Summit made recommendations on increasing recruitment. They attempted to position medical genetics as an ideal choice for students seeking an academic career. Other goals coming out of the Summit were to seek NIH funding for Centers of Excellence in medical genetics training and to enhance the visibility of medical genetics by working directly with resident and medical student advisory groups. There also was recognition of the need to strengthen core training issues, as well as to partner with other medical specialties. The second Banbury Summit, held recently, continued to address these issues, and a report on their findings was in press.

Dr. Fries said her practice was guided by the three "R"s: the extent of Recognition by other professionals, factors affecting the Referral process, and the lack of Medicaid Reimbursement. She also described the difficulties of using family history in diverse medical settings. Due to complex socioeconomic and cultural issues, obtaining accurate family history information across demographics was very difficult, even for experienced genetics providers. Immigrant populations may have minimal information on their parentage, as well as problems with literacy and language. Medical issues in the family might not be discussed because of taboos, or may be unknown. Dr. Fries stated that a key area of focus should be the development of tools and education across the demographics of language, culture, and literacy.

Dr. Fries described key professional organizations in medical genetics, all of which recognize the importance of education. In 1991, the American College of Medical Genetics (ACMG) was founded, which provides education, resources, and a voice for the medical genetics profession. ACMG makes genetics services available to improve the health of the public. The organization was in the process of developing 10 video telecasts so that people could see what geneticists actually do. ACMG was also revising medical genetics residency curricula. They were expanding point-of-care reference systems using ACT (ACTion) sheets for metabolic conditions in response to expanded newborn screening (NBS) programs. Positive NBS findings can be very upsetting to families; the ACT sheets were providing accessible, reliable information.

The American Society of Human Genetics (ASHG) is a broad organization that focuses on an overall understanding of genetics and attempts to decrease the public's fear of genetics. They developed programs geared for grades K through 12, including GenEdNet.org, which had a database of genetic standards for education at the K through 12 levels across all States. Other ASGH initiatives included DNA Day, essay contests, and a program called Genetics Education and Outreach. ASHG also was running an undergraduate workshop as part of every meeting they held, during which they incorporated students and undergraduate educators into the agenda, as well as high school educators from the local community.

The American Board of Medical Genetics (ABMG) is a certifying organization for professionals and training programs. It is very active in the maintenance of certification, which all physicians must meet.

Dr. Fries concluded with some recommendations. She said more research was needed on why people choose certain residencies. She felt that more knowledge of medical genetics could increase the level of interest in that specialty. She suggested a sponsorship program, much like those that sponsor residents who serve in inner cities or rural communities after their training. The issue of reimbursement was another area she said was in need of scrutiny. Dr. Fries closed by stating that education is not enough; what is learned must be put into practice.

**Question-and-Answer Session**

Dr. Williams addressed ACMG's positioning of medical genetics as ideal for students seeking an academic career. He noted that there were many opportunities in the private sector as well, and said he believed the private sector was underrepresented at the Banbury Summits. He stated that there was more money and were more job opportunities in the private sector, as well as more need. Dr. Fries agreed.

Dr. Khoury addressed the concept of evidence-based medicine, stating that the average practitioner needs guidelines and criteria. He suggested that as long as the genetics community continued to sell the genetic services model, which applied only to a fraction of genetic information, a larger market might be missed, i.e., that which allows interpretation of decoded genetics, genome profiles, combinations of genetic risk factors, and pharmacogenomics. Dr. Fries stated that one key to moving forward would be determining the circumstances under which insurers would support evidence-based medicine. She described an insurer that would not reimburse her for a complex genetics consultation; they would only reimburse a moderate consultation. She said this raised the question: What do you call “moderate” and what do you call “complex”? Dr. Williams suggested looking at the issue from a systems perspective, which is something that payers also want. He said the economic argument from a systems perspective is to approach issues the right way, so that money and valuable resources are not used on things that do not add value.

Dr. Willard pointed out that that medical genetics is not a growth industry, unlike genetics and genomics, for which there is great excitement and ready consumers. Other medical specialties recognize that they need to incorporate genetics and genomics. There is less recognition of the specialty of medical genetics as a profession that deals with people who have genetic disorders. He stated that evidence-based education could tell the field where to steer educational efforts, and that effort could be separated from the smaller, but equally important task of recruiting medical geneticists to deal with genetic syndromes.

Dr. Tuckson thanked Dr. Fries and introduced Ms. Angela Trepanier from the National Society of Genetic Counselors, who was also a program director of a genetic counseling graduate program.

**Meaning of Family History**
**Angela Trepanier, M.S., CGC**
**Co-Director of Genetic Counseling Graduate Program**
**Department of Molecular Medicine and Genetics**
**Wayne State University**

Ms. Trepanier addressed genetic counselors' roles in promoting the integration of genetic services into primary care. She identified three critical issues. The first was the need for agreement with regard to definitions of commonly used terms, such as "family history" and "genetic counseling." The second was the recognition that integration of genomics, genetics, and health care was an expanding and moving target. For this reason, she noted that it was timely to revisit the SACGHS 2004 resolution. The third issue was that there is no "one-size-fits-all" solution for integrating genomics into any health care profession.

Ms. Trepanier displayed a list of genetic counseling services, which are used selectively, based on the needs of the individual. She described the family history component of genetic counseling services, which attempts to elicit an appropriate and inclusive family history by asking targeted questions based on an understanding of the genetics, natural history, and features of the conditions being ruled in or ruled out. Interview skills are used to facilitate patient recall of symptoms and information on how the family has been coping with the condition in question.

She addressed the role of health care professionals without specialty training in genetics, stating that these roles must extend beyond identification and referral to include facilitation of the use of genetic services. Because there are not enough genetics health care professionals to address all potential uses, it is imperative that genetics be incorporated into primary care services. Ms. Trepanier said “practice factors” are critical to these efforts. These factors include what is known about the complexity of a disease’s genetics, testing, and management; the potential psychosocial impact; the complexity of decision making involved in dealing with the disease or condition’s risk; and the quality of the available data. “Provider factors” include their competencies in genetics, whether professional guidelines have been developed, and whether the provider adheres to the guidelines. Provider care can be limited by the practice setting, time constraints, and the provider’s own interest. Community factors also play a role, i.e., the availability of genetic services in the community, the community's willingness to utilize these services, the community's access to information about genetic risk, and whether insurance reimburses for services.

Genetic counselors developed a two-pronged approach to integrating genetics into primary care. The first prong included increased training and continuing education of genetic counselors, planning additional educational programs, and promoting the quality of the credential. The second prong related to educating health care providers and the public about genetics. Ms. Trepanier stated that there had been a slow increase in the number of genetic counselor trainees entering graduate programs since the inception of the American Board of Genetic Counseling (ABGC) in 1993. The number of trainees increased from 495 to 2,437. The number of programs increased from 18 in 1993 to 31 in 2007. The number of certified genetic counselors has increased by 1100 since 2004. Ms. Trepanier noted that attempts were being made to improve cultural diversity in the profession. She also described efforts to improve credentialing, licensure, and Federal recognition. The ABGC planned to conduct a practice analysis in 2008 that would help validate the certification exam and make it stronger. In the area of State licensure, 7 States passed licensure bills, 5 additional States introduced bills, and 13 had begun the process. At the Federal level, the National Society of Genetic Counselors (NSGC) was pursuing Federal recognition of genetic counselors by drafting legislation that, if passed, would amend the Social Security Act so that CMS would recognize genetic counselors as health care professionals.

Ms. Trepanier stated that genetic counselors had the training, expertise, motivation, and track record to be key providers of genetics education. Genetic counselors were increasing their efforts to educate other types of health care trainees and professionals by speaking to lay and community groups; organizing conferences; coordinating or serving on advisory boards; developing genetics curricula; serving on committees; and developing brochures, pamphlets, and videos. NSGC developed a speakers’ bureau, devoted an issue of the *Journal of Genetic Counseling* to genetics education, and obtained representation on key groups that were investigating how to incorporate genetics into health care.

Ms. Trepanier recommended that SACGHS not only support training of other health care professionals in genetics, but promote and support initiatives to increase the genetics professional work force and its diversity and cultural competence. She said this could be achieved by supporting the development of genetic counseling programs; providing scholarships to support matriculating students from underrepresented minority applicants; and supporting initiatives to increase the number of M.D. geneticists, laboratory geneticists, and genetic nurses. She closed by stating that she would submit comments on the SACGHS draft oversight report in writing.

**Question-and-Answer Session**

Dr. Tuckson suggested that all the players in the field of genetic counseling come together and decide on one board of competency certification. This would resolve the problems resulting from many different accrediting bodies having dueling accreditation criteria.

He introduced Mr. Toby Citrin of the Center for Public Health and Community Genomics in Michigan.

**Genetics Education and Training for the Public Health Work Force**
**Toby Citrin, J.D.**
**Adjunct Professor of Health Management and Policy**
**Director of Community-Based Public Health**
**University of Michigan**

Mr. Citrin noted the importance of the distinction between the terms “genetics” and “genomics” in the field of public health. He said it was extremely important to use the genomics paradigm, because it fit well with the ecological model of causation of health and disease, which was increasingly being used in the teaching and practice of public health. He pointed to CDC's website for the National Office of Public Health Genomics as providing a useful definition of genomics. Mr. Citrin noted movement away from viewing genetics as a separate, autonomous field and toward genomics as a component of all fields of public health teaching and practice.

He stated that the extent to which genetics or genomics were playing a role in the practice of public health was still quite small. Current practice encompassed traditional newborn screening programs, expanded genetic testing, some use of family health history in prevention programs for chronic disease, and early signs of acceptance by some health departments concerning health education in genomics. Indications were that in the future, there would be a growing need for knowledge of genomics in public health practice to individualize public health. That is, increasing knowledge of relative risk for an individual would inevitably shift the design and implementation of public health programs. Mr. Citrin predicted that the process of translation of research into methods and interventions would strengthen this shift and be useful in improving population health. He cited Dr. Khoury’s recent article in *Genetics in Medicine*, which described a four-step process that he said applied to public health interventions: gene discovery to health applications, applications to evidence-based guidelines, guidelines to practice, and practice to health impact.

In 2003, an Institute of Medicine (IOM) report, "Who Will Keep the Public Healthy?" identified genomics as one of eight content areas that needed to be taught to every student of public health, in addition to the traditional core areas of public health education. Mr. Citrin stated that Departments of Epidemiology were adding courses in genetic epidemiology, Departments of Biostatistics were teaching statistical genetics, and courses in environmental health were increasing the teaching of genetics and its interrelationship with environmental harms and hazards. Less evident, but extremely important, was the advent of incorporating genomics into the teaching of public health policy and the ethical, legal, and social implications of genomics within Departments of Health Management and Policy. There had also been a significant increase in the incorporation of genomics into the teaching of health behavior and health education.

Mr. Citrin addressed the barriers affecting the incorporation of genomics into public health teaching. He stated that academe commonly resists significant changes in curriculum. There was also insufficient time in the classroom to convey the most basic information necessary for public health professionals, causing

resistance to the addition of more content. A lack of expertise on the part of most faculty members was making incorporation of genomics difficult and contributing to a lack of recognition of the significance of genomics in public health. Some were antagonistic to the teaching of genomics because they believed less attention would be paid to social and environmental factors. Other barriers to genomics in the practice of public health included tight budgets, new requirements with respect to preparedness for bioterrorism and communicable diseases, a narrow view of genetics, and a lack of evidence-based, off-the-shelf tools based on genetics research and seen as useful to public health professionals.

Mr. Citrin described facilitators of the integration of genomics into public health. Chief among them was the CDC's National Office of Public Health Genomics, which was providing information through workshops and trainings. The Office also funded two Centers for Genomics and Public Health, one at the University of Washington and one at the University of Michigan, with which he was affiliated. The Centers were committed to expanding the knowledge, training, and utilization of genetic tools and information in public health practice. CDC was also funding four States (Michigan, Minnesota, Oregon, and Utah) to develop comprehensive genetics and genomics model programs that would work in State-level public health departments. The American Public Health Association (APHA) had recently formed the Genomics Forum, a group of over 200 public health professionals, community people, and academics interested in working together to further genomics within the public health framework.

Other facilitators were attempting to standardize competencies in public health teaching and practice. The CDC launched and funded an effort resulting in a set of genomics competencies for the public health workforce. The Education Committee of the Association of Schools of Public Health developed a set of competencies for the Master's of Public Health degree, which were advisory only and did not include sanctions or requirements. One of its 10 competencies was to explain how genetics and genomics affect disease processes in public health policy and practice. Mr. Citrin said the launch of a new examination for a certificate in public health was planned for August of 2008. It would apply to people who already had a Master's, but wanted a form of credentialing based on a standardized set of competencies in public health.

Mr. Citrin stated that hundreds of sources of training materials on genetics and genomics were available online, although no comprehensive compilation of these courses had taken place. The Genetic Alliance was undertaking an effort to list and codify online trainings and provide a sense of the level of competency they addressed. The Network of Public Health Training Centers developed a searchable website that identified genomics courses given by public health training centers.

Mr. Citrin noted that very little progress had been made in diversifying the public health work force that incorporates genomics. He said the growing diversity of the student population in schools of public health was not represented in genomics courses. For public health genomics to achieve its potential, the field would have to be more representative of the population that needs public health interventions.

Mr. Citrin closed with several recommendations. He said that schools and health departments should implement the recommendations on genomics published in IOM reports. He noted that the field needed to develop a way to systematically gather data on the extent to which genomics is truly included in the teaching of public health, not just labeled as such in course titles. He proposed a sharing of models of genomics teaching as a way to address the lack of competency by many faculty members. Mr. Citrin said that consideration should be given to having genomics identified as a standard for accreditation in schools of public health by the Committee on Education in Public Health (CEPH), the accrediting body. Public health education also needed to increase the focus on genetics and on the ethical, legal, and social implications of genetics. Mr. Citrin's final recommendation was that CDC broaden the network of

Genomics in Public Health Centers on a regional basis to serve the needs of health departments throughout the country.

Dr. Burns McGrath stated that the next four discussants would provide perspectives from various fields working in genomics. She introduced David Wilkinson from the Department of Pathology at Virginia Commonwealth University.

**Additional Perspectives**

**Laboratorians**
**David S. Wilkinson, M.D., Ph.D.**
**Professor and Chair**
**Department of Pathology**
**Virginia Commonwealth University**

Dr. Wilkinson addressed the state of genetics education among clinical laboratory personnel. He stated that the core of the workforce in clinical laboratories consists of medical technologists, also referred to as clinical laboratory scientists. They are trained, at a minimum, at the baccalaureate level. Programs in medical technology/clinical laboratory sciences are accredited by the National Accrediting Agency for Clinical Laboratory Sciences. Their standards specifically require training in genetics, molecular biology, and molecular diagnostics. The exact amount of time required on these topics or the details of the content are not specified. They generally do not have a requirement for any specific course in genetics. Although these personnel are well grounded in the basics of genetics, Dr. Wilkinson said they were not ready to perform the sophisticated level of testing required in a high-complexity laboratory, such as cytogenetics or molecular diagnostics. They require significant on-the-job training.

Dr. Wilkinson commented on medical student education. He noted that about 77 percent of all genetics course work takes place in the first year of medical school. There is minimal education in genetics in the third and fourth years of medical school, with some additional training in the clinical years. The United States Medical Licensing Exam (USMLE) is administered in three steps. The first step deals with the basic sciences and is given toward the end of the second year of medical school. The second step, clinical sciences, is given in the fourth year of medical school and focuses mainly on clinical education. USMLE was considering compressing steps one and two into one exam in the fourth year of medical school to increase the requirement for students to retain basic science information into their fourth year of medical school. Most basic science departments, however, did not want to see the step one exam eliminated. Dr. Wilkinson felt this issue should be studied carefully before a change was made.

Addressing graduate medical education, Dr. Wilkinson stated that the content of genetics education in residency training programs varied significantly depending on the residency. The governing bodies for the content of residency training programs are the residency review committees (RRCs), which operate under the auspices of the ACGME. The RRC for pathology specifically requires training in cytogenetics, molecular biology, and molecular diagnostics, although it does not specify the exact amount of time required or the content. The experiences of pathology residents varies depending on the specific training program. There is a subspecialty fellowship in molecular genetic pathology that is jointly administered by the American Board of Pathology and ABMG. This 1-year fellowship is devoted entirely to genetics, including exposure to genetics counseling and molecular diagnostics.

The final step in the continuum of medical education is continuing education. The College of American Pathologists (CAP) is very concerned about education and training in molecular biology and genetics.

Within the College, a cluster of committees focus on pathology and genetics. Two of these committees are jointly staffed by members of CAP and members of ACMG: the Biochemical and Molecular Genetics Resource Committee and the Cytogenetics Resource Committee. They work to bring these two medical specialties together to oversee the development of new products, as well as ongoing education. Other committees focus on histocompatibility, microbiology, and the genomics of cancer. The CAP committees manage the development of the College of American Pathologists and Accreditation Checklist. This checklist is one method for obtaining CLIA accreditation. Laboratories use checklists to ensure that they are compliant with CLIA. Since CLIA regulations have governance over all clinical laboratories and clinical testing, including genetic testing, they form a strong foundation for ensuring the quality of clinical laboratory testing in all areas. The CAP committees manage, create, and evaluate proficiency testing (PT) programs for specific areas within genetic testing, which is an important aspect of the CLIA program, which mandates PT. The CAP committees also generate educational programs for practitioners in the area.

Dr. Burns McGrath thanked Dr. Wilkinson and introduced Mr. Michael Rackover, who represented physician assistants (PAs).

**Physician Assistants**
**Michael A. Rackover, PA-C, M.S.**
**Program Director and Associate Professor**
**Physician Assistant Program**
**Philadelphia University**

Mr. Rackover represented the four physician assistants organizations: the American Academy of Physician Assistants (AAPA); the Accreditation Review Commission on the Education for the Physician Assistants (ARC-PA), which is the accreditation body; the National Commission of Certification of Physician Assistants (NCCPA), which is the certification and testing body; and the Physician Assistant Education Association (PAEA), which represents educators. He noted that these organizations had met recently to address the integration of genetics into clinical practice. The meeting was attended by the Executive Directors and Presidents of the individual organizations to create a top-down model for moving forward.

Mr. Rackover stated that there were 64,000 physician assistants in clinical practice. Gender representation was 38 percent male and 62 percent female. Twelve percent of PAs in practice were minorities, although those studying to become PAs included 23 percent minorities. Long-term goals for the profession included 90,000 practitioners by 2010, and 115,000 to 130,000 practitioners by 2020. PAs are part of most health care teams, as they work in HMOs, group practices, hospitals, with outpatients, and in nursing homes.

Continuing medical education credits (CMEs) are available in specific aspects of genetics education. AAPA received a grant from HRSA to work with NCHPEG on genetics in the physician assistants practice. In 2007, there were about 139 PA programs across the United States; in 2006, over 4,800 students graduated. Mr. Rackover noted that there are established models for competencies.

A 2007 PAEA survey of genetics education and PA programs across the country received a 75 percent response rate. The goal of the survey was to determine how genetics was being taught in physician assistants programs, what genetics content was being covered, and faculty needs for supporting a genetics curriculum. It was determined that the greatest barrier to genetics education was a lack of time. However, 62 percent of the programs planned to change their approach to teaching genetics in the near future.

Mr. Rackover stated that in September 2006, ARC-PA added new accreditation standards, including instruction in the genetic and molecular mechanisms of health and disease. NCCPA was also working on education activities concerning genetics. They were looking at exam content and beginning to code new items on the exam with a genetics code, when applicable. A new exam writer with experience in genomics was expected to be hired in 2008. Mr. Rackover closed by stating that the four major PA organizations were working together on a methodology to promote continuing education for educators in genetics, ensure that genetics was taught in the classroom and in clinical education, and ensure that certification and accreditation encompassed genetics.

Dr. Burns McGrath thanked Mr. Rackover and introduced Ann Cashion, who was representing the International Society of Nurses and Genetics (ISONG).

**Nurses in Genetics**
**Ann K. Cashion, Ph.D., R.N.**
**ISONG President**
**Chair and Associate Professor, Acute and Chronic Care Department**
**Robert Wood Johnson Executive Nurse Fellow**
**Director, Center for Health Evaluation and Lifestyle Promotion**
**University of Tennessee Health Science Center**

Dr. Cashion described how nurses obtain genetic training. She stated that two key education programs include the National Institute of Nursing Research (NINR) NIH Summer Genetic Institute, which had 121 graduates; and the Genetic Education Program for Nurses, which was conducted through Cincinnati Children's Hospital. Both programs trained nurses who went back to their individual institutions throughout the United States and incorporated genomics into their teaching models. Continuing education opportunities for nurses were also available through professional organizations; primarily through ISONG; the Oncology Nursing Society; and women's health, pediatric, and developmental organizations.

One of the areas in which gaps were found in genomics education for nurses was in faculty training. Dr. Cashion said ISONG published, “Genetic and Genomics Nursing Scope and Standards of Practice” through the American Nurses Association (ANA) to help identify the varying levels of competencies among genetics nurses in the field. Another important resource was “Essential Nursing Competencies and Curricular Guidelines for Genetics and Genomics,” which describes what practicing nurses should know about genomics. Dr. Cashion pointed out gaps in instructional resources, such as existing continuing education programs (CEs), which must be adapted to meet the instructional needs of faculty. The challenge was to decrease the burden imposed by adding more content to a dense curriculum, while allowing for academic freedom and creativity. Once appropriate instructional resources were created, they would need to be maintained and updated, in part through a peer review process.

ISONG also wanted to maximize the use of interdisciplinary genetics nursing courses and share resources among universities without increasing costs to students. Dr. Cashion stated that the Southern Research Educational Board (SREB) had a model for this type of resource sharing. ISONG was in the process of developing a molecular genomics course with some clinical content that would be taught online for students from various universities.

Dr. Burns McGrath thanked Dr. Cashion and introduced Ms. Judith Benkendorf of ACMG to offer her perspective on workforce issues.

**Workforce Issues**
**Judith Benkendorf, M.S.**
**Project Manager**
**American College of Medical Genetics**

Ms. Benkendorf stated that the genetics workforce was very small, unequally distributed geographically, and not representative of the diversity of the U.S. population. She provided supporting data from ABMG, ABGC, and an ACMG workforce study. She said there were approximately 4,700 individuals holding certificates in a medical genetics profession; about half were genetic counselors and the other half were M.D.s and Ph.D.s certified by ABMG. Thirteen percent identified with minority populations, with the predominant group being Asian. Genetic counselors were the fastest growing cohort, comprising about half of the workforce. Only about six percent of genetic counselors were men and nine percent of genetic counselors represented minority communities. There was approximately one genetic counselor per 127,000 people in the United States.

M.D. geneticists numbered less than 0.02 of all physicians in the United States. There were about 1,100 active clinical genetics physicians in the country. A recent survey conducted through the ABMG by ACMG indicated that these individuals spent only 45 percent of their time seeing genetic patients. This means there was one clinical geneticist per 560,000 citizens. The ideal would be one full-time geneticist for 250,000 people.

Ms. Benkendorf emphasized that the medical genetics workforce situation was critical. The services workforce was not expected to meet patient demand within the next few years because young physicians were not entering the field. At least 17 States were identified as having an inadequate number of geneticists. Metabolic geneticists were the most critically needed because of expanded newborn screening and the continual influx of new affected individuals who will require lifelong chronic disease management and treatment. In addition, 20 percent of metabolic geneticists were expected to retire by 2008. Ms. Benkendorf stated that approaches to remedy this problem must be multi-pronged. Federal funding was needed for training medical geneticists and training and recruitment efforts must improve. ACMG had recently approved creation of the first clinical geneticist subspecialization: the medical biochemical geneticist.

Ms. Benkendorf said the Banbury Summit in 2006 attempted to define the domain of medical genetics practice and they planned to publish the resulting principles in *Genetics and Medicine*. She highlighted several of the key principles. Medical genetics is dedicated to improving the health of individuals, families, and communities; and geneticists will treat patients across the life span for conditions involving all organ systems. The field has a public health interest and will respond to the rapid pace of genetic discoveries with new educational and training and practice paradigms. Practitioners are interested in the translation of new technologies into health care, monitoring outcomes, and patient management.

Ms. Benkendorf described some steps being taken to move the field forward. She said ACMG created a tagline, "Translating Genes into Health," and was working on a branding campaign with the help of a public relations and media advisor. She quoted Dr. Hunt Willard, a former ASHG president, as pointing out the need to “open the tent,” i.e., the field of medical genetics needed to expand joint training programs with pediatrics, internal medicine, pathology, neurology, and other fields. This requires the teaching of gene-environment interactions and health care throughout the life span. The field must consider how genetic services would be distributed based on complexity, taking into account needs in primary care, specialty care, and the role of the medical geneticist. Ms. Benkendorf said it would be important to monitor consumer genetics and the personalized medicine movement. To reach rural areas with new

technologies, telemedicine initiatives were taking place through ACMG's National Coordinating Center and the Regional Genetics and Newborn Screening Collaborative. Other efforts would include new training modalities, integrating the point of care and decision support tools into the electronic medical record, and anticipating future needs so that the workforce could grow.

Dr. Burns McGrath thanked Ms. Benkendorf and opened up the floor for questions for all speakers.

**Roundtable Discussion**

Dr. Tuckson asked the Committee to keep several questions in mind as they discussed the information presented by the speakers. He noted that the problems described might be related to such factors as genetic exceptionalism, a lack of expertise in various disciplines, or a lack of coordination of the various infrastructures across disciplines. He posed the question of whether patient care was being compromised. He also raised the issue of what the Secretary could do to address existing problems. He noted the relationship of the challenges presented by the speakers to the draft oversight report and the coverage and reimbursement report, which included a section on appropriate reimbursement for genetic counseling, including the role of CMS. Finally, he asked the Committee to consider what genetics health professionals should do for themselves, both through advisory boards such as SACGHS, and through their own specialty societies and boards.

Mr. Miller suggested including people with disabilities in discussions of diversity in the workforce. This medically underserved population is underrepresented in the health care professions in general, and particularly with respect to genetics. He also asked if SACGHS could play a role in bringing groups together to talk about the qualifications of genetics professionals.

Dr. Khoury asked how the translation of genetic information into practice could be accomplished, given the lack of an adequate workforce. He asked what the role of new genetic professionals should be in translating genes to health, and how the new workforce could embrace evidence-based medicine. He made the point that payment for genetic services would not take place without an evidence base indicating that these services improved health. Dr. Fries stated that because genetics became a residency-based specialty very recently, the field did not have a large body of practice information. The evidence base would have to be developed, in part, by incorporating information from other specialties' practices and from best practice guidelines based on a limited number of experiences with patients. She suggested setting up large, sponsored trials based on innovative strategies. She suggested that SACGHS could be influential in the funding and support of those strategies.

Dr. Kahn stated that the most important thing the Secretary could do to help integrate genomics into daily practice was to focus on decision support in electronic health records (EHRs) and in practices that can obtain decision support tools through the Internet, even if they do not have EHRs. Ms. Benkendorf noted that the next generation of newborn screening ACT sheets she described would be integrated into electronic medical records as a point-of-care education tool, and this effort would be evaluated. She said ACMG had obtained funding to convene a meeting of EHR industry professionals to talk about decision support tools.

Ms. Aspinall stated that there were two elements missing from the discussion: industry representation and a focus on the window of opportunity available because many physicians were already using or planned to use EHRs. She said a new system would need to be developed to accommodate new practice guidelines, tests, and other information. Ms. Aspinall also asked if the organizations and professions

represented were actively collaborating and sharing information. Mr. McInerney replied that all of the organizations present interacted with one another. They also welcomed input from other groups.

Dr. Licino asked how well prepared the average genetics professional would be to interact with consumers who had responded to direct-to-consumer (DTC) marketing and received information about their genome that was not really significant in terms of actual risk for genetic disease. He asked if professionals should be equipped to deal with these situations. Mr. McInerney stated that genetics professionals are equipped to handle these situations, but the average primary care provider would not be. He noted the opportunity to talk about these situations when educating medical students. As an educator of undergraduate nursing students, Dr. Cashion said she often taught genetics by visiting various websites for the latest information and encouraging her students to be lifelong learners.

Mr. Citrin added several comments from the public health perspective. He stated that a larger faculty in schools of public health was not needed to incorporate genomics. Rather, faculty members should incorporate genomics into the subjects they already taught. He said the same was true of public health departments. He framed the issue as a training and education challenge, not a workforce challenge, and noted that the integration of genetics with all the other factors of health and disease could prevent a worsening of disparities over time as genetic tools become more widely available.

As he ended the session, Dr. Tuckson stated that the issues raised would require more deliberation by the Committee. He suggested that a Task Force be formed to investigate challenges in education and training. The Task Force members and scope of work would be discussed in more detail later in the meeting.

**Recognition of SACGHS Members**

Dr. Tuckson introduced Rick Campanelli, the Secretary's Counselor for Science and Public Health. Mr. Campanelli thanked Chira Chen, Cynthia Berry, and Hunt Willard for their service to SACGHS, as they were rotating off the Committee.

Dr. Tuckson announced that on November 5th, Dr. Francis Collins received the Presidential Medal of Freedom, the Nation's highest civil award, for his leadership in the Human Genome Project. Dr. Tuckson expressed the Committee’s appreciation to Dr. Collins for his representation on SACGHS. Dr. Collins stated that he appreciated the collegiality of the Committee and enjoyed being part of their deliberations.

Dr. Tuckson introduced the oversight session and turned the floor over to Task Force Chair Andrea Ferreira-Gonzalez.

**Session on Oversight of Genetic Testing**

**Overview of Session**
**Andrea Ferreira-Gonzalez, Ph.D.**
**Task Force Chair, Oversight of Genetic Testing**

Dr. Ferreira-Gonzalez stated that the draft oversight report was undergoing public review until December 21. She explained that the session would focus first on an international analysis of regulatory gaps in the oversight of genetic testing and models to address those gaps. Following this presentation, various stakeholders would have the opportunity to comment on the draft report.

Dr. Ferreira-Gonzalez reviewed the charge from OS that shaped the report's content. The report responded to eight questions about key measures of validity and quality of genetic testing technologies and processes to assure their safety and effectiveness. The Secretary asked the Committee to consider Government and private sector solutions to gaps in oversight and advised SACGHS to focus on the future, so that the recommendations would be forward-looking. The Oversight Task Force was comprised of 33 members including SACGHS members and other experts from Federal agencies and the private sector. The draft report that was released for public comment was organized into 7 chapters and put forth 16 recommendations. The comment period was scheduled to end on December 21, 2007, after which the comments would be analyzed and incorporated into the report, as appropriate. Final recommendations would be submitted to OS by the end of February 2008, with the final report formally submitted in April 2008. Dr. Ferreira-Gonzalez stated that the full Committee would have the opportunity to review and provide further input on the report before it was finalized. She introduced Mr. Stuart Hogarth and Dr. David Melzer. Mr. Hogarth is a visiting Research Fellow at the Institute for Science and Society at the University of Nottingham. Dr. Melzer is a professor of epidemiology and public health at the Peninsula Medical School in Exeter, England.

**International Perspectives on the Oversight of Genetic Testing**
**David Melzer, M.B., B.Ch., M.Sc., Ph.D., FFPHM**
**Professor of Epidemiology and Public Health**
**Peninsula Medical School, Exeter, England**

**Stuart Hogarth**
**Visiting Research Fellow**
**Institute for Science and Society, University of Nottingham**

Dr. Melzer stated that he and Mr. Hogarth would discuss the results of a policy research project funded by the U.K. Wellcome Trust that focused on the following question: How do we ensure that doctors, patients, and health care systems make informed decisions about the use of new genetic tests? They explored three phases of evidence development: 1) evidence generation, which addresses the incentives and infrastructure required to generate a robust evidence base for new tests; 2) evidence evaluation, which addresses the regulatory mechanisms for independent evaluation of the evidence for new tests; and 3) evidence sharing, which addresses systems for ensuring that doctors, patients, health care policymakers, and reimbursers have access to accurate and comprehensive information, presented in a way that can be readily understood. The project involved individual interviews, workshops, and focus groups in Europe and the United States and contacts with people in Canada and Australia.

Dr. Melzer stated that the Wellcome Trust is an independent research philanthropy that has no connection with drug companies. The project was completely independent and had no conflicts of interest. Funding came from NIH and from U.K. research grants.

Dr. Melzer described what he called the genetic testing of the past, for family-based, often high-penetrance disorders, for which the clinical significance of markers was fairly clear. However, he stated that the field was moving into a much different situation, in which there is a statistical association between claimed markers, and the marker is more common in the cases than the controls. Sometimes the markers are only present in a small proportion of cases and some of the controls have the markers as well. Dr. Melzer noted the large number of recent genome-wide association studies, citing the Wellcome Trust Case Control Consortium, which published 28 independent signals for eight conditions. Breakthroughs occurred in age-related macular degeneration, asthma, restless leg syndrome, and Type II diabetes.

Dr. Melzer described his study at Exeter on Type II diabetes, during which he worked with 2,000 cases and 3,000 controls and genotyped 500,000 markers across the genome. Massive statistical associations were found, and about 12 were robustly proven. He stated that the important message for policymakers and regulators was that there were many more associations about to be discovered. He cautioned that many of the new breakthroughs were relatively modest, indicating increased risk levels at about 10 to 15 percent. He said it was too early to apply much of this information to clinical use.

Dr. Melzer noted that many of the tests marketed to consumers failed to replicate in large, decisive studies. The overall predictive value of these tests for health outcomes was unknown. Nevertheless, the public may be tempted to use them for paternity testing, pre-implantation testing, macular degeneration, or myocardial infarction testing. Dr. Melzer noted that most studies for these tests were conducted on Caucasians and there was very little evidence on their applicability to minority groups. He then turned the presentation over to Mr. Hogarth.

Mr. Hogarth provided information on several companies that were developing genetic tests and moving into the market very quickly. The U.S. company InterGenetics launched the OncoVue test in Europe. It is a polygenic test intended to inform women about their risk of breast cancer by using a panel of markers and interpretive algorithms. deCODE genetics, an Icelandic company, was marketing deCODEme services directly to consumers. These services include susceptibility testing for 17 common diseases, including age-related macular degeneration, breast cancer, asthma, colorectal cancer, multiple sclerosis, heart disease, and prostate cancer. The list of genetic risk assessments will be continually updated as new discoveries are made. Similar services are available from 23andMe, Navigenics, and Smart Genetics.

Mr. Hogarth said the market was operating on an international level. Although deCODE is based in Iceland, its tests are available in the United States. InterGenetics is U.S.-based, but its OncoVue test was launched in the United Kingdom. Genetic Health offered a range of susceptibility tests from its base in London, but the tests were being provided by an Austrian company called Genosense. This Austrian company was also offering its tests through intermediaries in a number of other countries, including Canada and the United States.

Concerns had been expressed about these tests on a number of fronts. The British Society of Human Genetics believed that the tests being offered by Genetic Health were essentially useless and were being promoted with unsubstantiated and overblown claims. Mr. Hogarth pointed out that there had been longstanding concerns about genetic tests moving into the clinic too fast, particularly tests for common diseases. He cited BRCA testing as the most high-profile example of a test for which the claims at market launch went far beyond the data behind the test. Such policy concerns in the United States, Canada, Australia, Europe, and other countries resulted in an examination of oversight mechanisms by a series of high-level committees. One of the key conclusions that came from the resulting reports was that genetic tests should not enter routine clinical practice unless they are independently evaluated.

Another concern requiring attention was the need to communicate comprehensive, accurate information to patients and doctors about genetic tests. Mr. Hogarth framed this concern as “regulation by information disclosure,” which he said was a very popular concept in the consumer protection field. In some cases, companies were not telling people which single nucleotide polymorphisms (SNPs) and genes they were actually testing. In the case of Genetic Health, they maintained complete secrecy about their gene panel.

Mr. Hogarth stated that the oversight debate had also started a conversation about what needed to be evaluated and the categories of information needed by patients and doctors. He noted that there was no well functioning system that allowed for more independent evaluation of tests and better information for

doctors and patients. No existing regulatory systems had the necessary enforcement mechanisms, and all had many gaps. He addressed the gaps in regulatory systems from an international perspective, which he said differed by country.

Mr. Hogarth explained that in the United States the primary gap in terms of premarket review is that FDA does not regulate laboratory-developed tests (LDTs) as medical devices. Recently, however, FDA identified a small subset of tests, known as in vitro diagnostic multivariate index assays (IVDMIAs), which would be subject to premarket review. The primary regulatory gap in Europe is that they classify nearly all diagnostic tests as low risk, making them exempt from premarket review. This classification includes all genetic tests except those for phenylketonuria (PKU). Europe's treatment of LDTs is very different than in the United States. In Europe, LDTs are considered medical devices, with some exemptions (e.g., health care institutions are not subject to device regulations). Canada's regulatory gap concerning LDTs is similar to the U.S. gap, as its authority over LDTs is unclear. Australia was revising its medical device regulations, which treated LDTs as medical devices and treated genetic tests as moderate risk, making most of them subject to premarket review.

Mr. Hogarth said the United Kingdom had a new system for evaluating single-gene tests within the National Health Service, the U.K. Genetic Testing Network. In addition, the U.K.'s National Screening Committee was looking at the regulation of commercial screening services, and the Human Genetics Commission (HGC) renewed its interest in the regulation of DTC genetic tests. A new report was forthcoming from the HGC.

Mr. Hogarth described developments in Europe. EuroGenTest, which consists of a network of clinicians and laboratory professionals, was working on quality assurance and other issues concerning the quality of genetic testing. The IVD device regulations were about to be revised, and discussions were taking place within the European Commission and member states. Mr. Hogarth stated that the agency responsible for drug regulation in Europe was the European Medicines Agency (EMEA), which was collaborating with FDA on pharmacogenomics issues. Europe had also been participating in international initiatives, such as the Organisation for Economic Coordination and Development's (OECD's) quality assurance guidelines for molecular genetic testing. The Council of Europe was working on a protocol for genetic testing that would address DTC testing and recommend that tests be offered with individualized medical supervision. Predictive tests for monogenic diseases and susceptibility tests would only be offered with counseling.

Australia completely revised its IVD regulations, in part to deal with the LDT issue. They also published guidance on the regulation of nutrigenetic tests, an international first. Canada issued guidance on PGx tests. Internationally, the Global Harmonization Task Force, a forum for device regulators, was trying to standardize IVD regulation. The International Committee on Harmonization (ICH) was working on PGx issues. Mr. Hogarth noted that Dr. Khoury, with international colleagues in public health genetics, was involved in the Human Genome Epidemiology Network (HuGENet).

Mr. Hogarth reiterated that the most significant development in the United States concerning premarket evaluation of tests and FDA's role was the IVDMIA guidance. He suggested that the guidance had correctly identified the area in which FDA intervention was most urgently needed and had brought clarity to FDA's position. He stated, however, that FDA should also consider its broader responsibilities concerning LDTs, as the guidance did not address most LDTs, including high-risk tests.

Mr. Hogarth stated that significant changes in the business of IVDs were underlying recent technological changes, clinical development, and scientific progress. He said it was crucial to understand this new business model when dealing with oversight issues. In the traditional model of the IVD sector, companies

held intellectual property (IP) platforms and tended to compete with one another. They developed different versions of testing for the same biomarkers. This model resulted in a very competitive industry with low profit margins compared to the pharmaceutical sector. With low profit margins, little protection of investment, and little experience or infrastructure for large-scale clinical validation, the traditional sector had not focused on large studies to demonstrate the clinical validity and clinical utility of new tests. A model with weak IP rights and biomarkers meant that there was no one party responsible for developing clinical data to ensure the clinical validity of a new test. Mr. Hogarth pointed out that there was actually a disincentive for large-scale clinical studies, because a manufacturer who made such an investment and brought a test to market would immediately be competing with other companies. Academic studies and professional advocates were filling the gap, often promoting tests on the basis of ad hoc experience. However, Mr. Hogarth stated that many companies in molecular diagnostics were disrupting the traditional business model. They started developing tests based on protection of the gene or the association with the disease, and the emerging market for gene expression and proteomic tests was often based on strong IP rights and biomarkers.

Mr. Hogarth stated that many of these companies were seeing significantly higher levels of reimbursement for some of their tests than under traditional diagnostics. Potentially, if stronger IP rights and biomarkers give a company a monopoly on a test and reduce competition, the company will have an incentive to generate clinical data. Companies were starting to develop tests, offer them on a monopolistic basis through their own reference laboratories or by licensing them to another company, and compete on the quality of their clinical data. Mr. Hogarth noted that if companies do not have incentives to generate clinical data, there is no point creating a better system for evaluation, because the data to evaluate will not exist.

Although there were some advantages to this new business model, it also posed some challenges. Many people had expressed concern that tests offered on a monopolistic basis were not subject to traditional peer review in the field. There was no opportunity for laboratory directors to try out a test and see its strengths and weaknesses firsthand. There was also concern that when a company had a significant investment in bringing a test to market quickly, it might make overblown claims for the test. In the absence of an effective oversight mechanism, there was no way for patients and doctors to distinguish between “good players” and “bad players.”

Mr. Hogarth presented six reasons for requiring premarket review for LDTs as medical devices: 1) They can pose the same risks as commercial tests; 2) LDTs are big business; leading companies are bigger than many kit manufacturers; 3) Small laboratories do not receive a CLIA exemption, so why should they receive an FDA exemption; 4) It is possible to do premarket evaluation of LDTs (e.g., New York State); 5) Premarket review of LDs is clearly the international trend (e.g., Europe and Australia); and 6) The business model for reference laboratory monopolies might pose risks. However, Mr. Hogarth acknowledged that applying statutory premarket review to all LDTs might be unduly burdensome, and he asked if a model of “one size fits all” could really work, particularly in the area of rare disease tests. He suggested that a range of alternative oversight options was needed to address problems in implementation. Previous recommendations from other committees came up against the need to balance evaluation, innovation, and access; a lack of clarity on the roles of different gatekeepers; the role and resources of FDA; and industry reluctance for enhanced oversight. He asked if there some way to develop a more comprehensive system of evaluation, while ensuring adequate protection to the public and encouraging innovation.

He suggested a number of solutions that came from his research with stakeholders across the spectrum, including industry, FDA, and patients' groups. One of the solutions was to focus premarket review on

truth in labeling. Another was to have a greater emphasis on postmarket controls and to clarify an appropriate role for various gatekeepers, which is linked to the idea of responsive regulation. Mr. Hogarth said that Government agencies, regardless of country, are not the only ones who have a role in gatekeeping. He said the draft SACGHS oversight report was addressing responsive regulation by analyzing different kinds of compliance mechanisms, including mandatory and incentive-driven, and voluntary and informal. When considering the three core functions of regulation (i.e., information-gathering, standard-setting, and enforcement/compliance), he said there are many ways that various entities can be involved in the process of oversight.

Mr. Hogarth addressed the issue of using oversight mechanisms to provide accurate, comprehensive information to doctors and patients. He said IVD device regulations should be primarily focused on premarket review of analytic and clinical validity, set clear evidence standards for market entry, monitor performance in the postmarket environment, and ensure truth in labeling and truth in promotion. IVD regulations should not deal with ethical and social issues, such as genetic discrimination; should not regulate clinical practice issues, such as informed consent; and should not evaluate clinical utility, which his research suggested was best left to health technology assessment and clinical practice guidelines. By focusing on premarket review and truth in labeling, regulation would take place through information disclosure. This minimalist approach would reduce the regulatory burden and pass the responsibility for risk management on to doctors and patients, allowing them to make informed choices about tests.

His research indicated that since doctors often will not have time to survey the literature on the quality of evidence that supports new tests, such information should be simplified, much as food labels provide easy-to-understand guidance to consumers. Mr. Hogarth suggested a simplified schema that would indicate where a test lies on the development spectrum, from research to well established clinical use. As an alternative, the schema could be based on evidence-based medicine standards, such as those developed by the Cochran Collaboration. The definition of a label could be expanded to ensure that those who offer tests provide information to clinicians and the general public, not just those in the laboratory setting. Test manufacturers and developers could post their labels online, along with sample reports of test results that showed reference ranges and other pertinent information.

Mr. Hogarth said labeling is an area in which there is a clear difference between test kits and LDTs. He said there is no regulatory equivalent of a label for an LDT, but LDT users should provide this information to the users. Although FDA had begun to address this issue in the IVDMIA guidance, Mr. Hogarth said more work was needed. He stated that regulators could facilitate information disclosure by making their device reviews and subsequent postmarketing data public. FDA was publishing review summaries on its website, in contrast to Europe, where such data was treated as confidential. Mr. Hogarth said that FDA could do more, such as making the information easier to find and presenting it in a more understandable way.

Mr. Hogarth described a minimalist approach to “premarket controls,” that is, all forms of oversight that exist once a test is on the market. For tests with a broad application, health technology assessments operated as an effective form of oversight and provided gatekeeping functions. As an example, the Roche Amplichip was approved by the FDA, but was subsequently subjected to a series of critical health technology assessment reports in the United States, Canada, and Europe. Mr. Hogarth also noted the important role of clinical governance. Many committees, including SACGHS, pointed out the need for increased use of and better funding for clinical guidelines. He stated that independent sources of information were becoming more common, such as the GeneTest website and Lab Tests Online.

Many concerns were being expressed by industry and other stakeholders about a possible enhanced role for FDA, and the agency was expressing concern about its ability to take on more work. Mr. Hogarth offered some alternatives to expecting FDA to do more. A data registry could serve as an alternative regulatory mechanism without placing an undue burden on test developers. Some stakeholders wanted a comprehensive registry that would provide detailed information about the tests provided by laboratories. Mr. Hogarth stated that this raised two issues: "Who could guarantee the quality of information?" and "Who could deal with complaints?" He suggested looking upon the role of FDA as a "meta-regulator," that is, FDA would have an overarching role and address complaints, and in certain instances, would be the guarantor of quality. A data registry could be managed and maintained by other parties. In the European model for IVD device regulation, tests are subject to premarket review by an independent third party. The Australian model also has adopted a system of third-party review, which takes place through professional pathology bodies. Mr. Hogarth suggested that FDA empower third-party review, with other agencies within the United States acting as third parties. He noted the systems used by New York State and the Collaboration, Education, and Test Translation (CETT) initiative, which developed a system for evidence-based introduction of rare disease tests.

Mr. Hogarth closed by reviewing his key points, stating that the United States must find ways to balance innovation and regulation through such efforts as regulation by information disclosure and the concept of responsive regulation and its tools, including a more flexible approach to premarket review and a greater emphasis on postmarket controls.

**Question-and-Answer Session**

Dr. Collins asked the speakers to comment on the value of a voluntary versus a mandatory registry. Dr. Melzer stated that in Europe, clinical information (e.g., identifying groups of patients, the purpose of tests, which SNPs are covered, and the scientific basis for the test) was not being provided voluntarily. Many companies are secretive. He expressed concern about the 5-year window for voluntary registration recommended in the draft oversight report, because he said the worst abuses would take place during the next 5 years. Mr. Hogarth asked why SACGHS was hesitant to recommend a mandatory system, stating that it was not unreasonable to expect a company offering a clinical test to summarize the analytic and clinical validity of the test, its likely clinical utility, the indications for its use, and other information. He said if that data could not be provided, the company should not be offering the test.

Dr. Teutsch asked the speakers whether a system would work if the information they described was mandatory and necessary for reimbursement. He asked for examples in which payers were involved in the scrutiny of the data. Mr. Hogarth pointed out that the role of reimbursers as gatekeepers does not apply in the area of DTC testing. He then cited the Amplichip as an example of an FDA-approved test that was followed by rigorous assessment of its clinical utility for reimbursement. Dr. Melzer stated that the reimbursement system in Europe worked differently because of their nationalized health services.

Dr. Williams asked the speakers about the idea of evaluation taking place in the context of the postmarket period, because clinical utility would either be demonstrated or not. He also commented on the international aspects of marketing tests. He suggested that the oversight report include a discussion of international issues, with an eye toward achieving some common goals and greater collaboration. He asked whether the speakers believed there were reasons for treating genetic tests as exceptional in a regulatory content.

Dr. Melzer said that research ethics problems were coming into play in situations where evaluations were taking place on the public's samples without their knowledge. Concerning the international aspects of

genetic testing, Dr. Melzer said these issues were under consideration by Europe's Harmonization Task Force. He stated that companies in various countries in Europe were eager for harmonization. They did not want to have to produce new evidence for different markets; they would prefer a common evidence requirement. He said his research team had debated genetic exceptionalism at length and that genetic tests in the United Kingdom were considered different in some respects. The regulatory system was harmonized with all other tests, but special committees were looking at genetic testing. He argued that from a public health standpoint, genetics should be seen as an opportunity to improve test regulation throughout systems and to get basic information to doctors and patients.

Mr. Hogarth added that there were many interesting examples of international cooperation, such as the OECD guidelines on quality assurance and FDA's work with EMEA on voluntary genomic data submissions and PGx tests. He considered it important to lower the burdens for companies by creating more consistent standards on the international level.

Dr. Ferreira-Gonzalez thanked Mr. Hogarth and Dr. Melzer. She introduced the public comment session on the draft oversight report and welcomed the first speaker, Ms. Sharon Terry.

**Public Perspectives on the Oversight of Genetic Testing**

**Sharon Terry**
**President and CEO, Genetic Alliance**

Ms. Terry described a Genetic Alliance September 2007 meeting on genetics that convened stakeholders, including the payer community, biotechnology and pharmaceutical companies, advocacy organizations, Government and health care agencies, academia, policy groups, and the provider community. Meeting moderators and interviewers facilitated discussions and no PowerPoint presentations were allowed. Some of the recurring themes included: tensions in the system caused by the move toward personalized health care, allocation of scarce resources, the need for public-private partnerships, reimbursement issues, management and sharing of data in biobanks, the transfer of genomic technology to the developing world, clinical evidence standards, intellectual property models, nondiscrimination legislation, expansion of the CETT model, the role of patients in the advocacy community, study design, regulatory authority for genetic testing and the role of Federal agencies, implementing new genomic technologies, characteristics of voluntary or mandatory data registries, medical records aggregation, the role of professional organizations, weighing costs and values, risk-based regulation, increasing PT without placing undue burden on laboratories, protection of the public from fraudulent and exaggerated DTC tests, and clinical utility.

The group arrived at a number of conclusions that would be published in a 60-page report in the winter of 2008. Key conclusions expressed the need for the following: additional NIH requirements on funding and standards along the basic and translational research pipeline, so that evidence standards could be achieved more effectively; more discourse with and responsiveness from the Federal agencies that have jurisdiction over genetic testing; coordination of jurisdiction and the activities of CMS, FDA, and other relevant agencies; clarity and predictability conducive to a growing and stable marketplace; a risk-based regulatory system, with a caveat that allowances be made for volume; oversight of DTC tests; increased public-private partnerships as a means for ensuring the pipeline of discovery; education at all points; outcomes data collection and clear evidence bars; a means for industry to rid itself of bad actors; and a mandatory registry established and managed by either a public-private partnership or by a Government agency.

Action steps were proposed for various groups in attendance. These included advocating for enhanced CLIA regulation; promoting a mandatory registry; convening summits on reimbursement issues, evidence and outcomes data, third-party review, and emerging models around genetic testing regulation; exploring the concept of various levels of risk; education of Congress, patients, and clinicians; supporting Federal nondiscrimination legislation; and examining global perspectives.

Dr. Telfair asked why the summits on the registry, reimbursement issues, and evidence and outcomes data were planned separately, since there was significant content overlap in these areas. Ms. Terry replied that the proposed summits would have great depth.

Dr. Collins asked for more detail on the group's thinking about the mandatory registry. She stated that the details were not fully fleshed out, but the general feeling was that FDA should house the registry, although a public-private partnership was a viable alternative. In the latter case, the registry might be managed by a professional society or a coalition of laboratories. One suggestion was that the registry could build on GeneTest and then be moved to FDA, with some input from NIH. The belief was that if the registry was completely voluntary, it would not be implemented. Dr. Ferreira-Gonzalez asked if some groups at the meeting were opposed to a mandatory registry. Ms. Terry said that some attendees had left the meeting by the time this discussion took place, but that no one present disagreed with the idea of a mandatory registry.

Ms. Aspinall asked about the concept of risk and how the group, at a basic level, thought about apportioning risk and potential harms or potential opportunities. Ms. Terry replied that an action item was developed to explore this area, because it was not thoroughly examined during the meeting.

Dr. Ferreira-Gonzalez thanked Ms. Terry and introduced Mr. David Mongillo.

**David Mongillo**
**Vice President for Policy and Medical Affairs**
**American Clinical Laboratory Association (ACLA)**

Mr. Mongillo commented on key areas of the draft oversight report. He said it was critical that CMS, as the agency responsible for CLIA, continue as the lead agency responsible for the oversight of laboratory developed genetic test services and that FDA should continue to have a significant role. He stated that as the report stressed, interagency coordination was fundamental to ensure that oversight was not burdensome and did not place unnecessary or duplicative regulations on clinical laboratories providing genetic test services. ACLA supported the report's recommendations for HHS to convene a workshop with relevant agencies and stakeholders to provide input on the development of a risk-based framework for the regulation of genetic LDTs, and they encouraged and supported the development of new and transparent models for private sector or public-private partnerships. The second area Mr. Mongillo addressed was the implementation and timing of the report recommendations on interagency coordination. He said that to allow for a well reasoned and orderly regulatory process, ACLA urged the Committee to include an important stipulation in the report, that is, the report's recommendations should be implemented and understood before the FDA's IVDMIA guidance was finalized or its analyte specific reagents (ASR) guidance enforced. The SACGHS recommendations could then inform further guidance and regulatory action. Finally, Mr. Mongillo said the section on effective communication and decision support was particularly noteworthy. ACLA pledged support for clinical decision support systems.

Dr. Ferreira-Gonzalez thanked Mr. Mongillo and introduced Ms. Patricia Goldberg.

**Patricia Goldberg**
**International Society of Nurses in Genetics (ISONG)**

Ms. Goldberg said her brief remarks were part of a longer statement that would be submitted by ISONG concerning the draft oversight report. She stated that ISONG was concerned about the lack of clinical validity and clinical utility of genetic tests being advanced as useful for common disorders, such as diabetes and hypertension. ISONG suggested that more attention be given by SACGHS to the interpretation and application of the genetic and genomic results obtained by DTC tests for these common disorders. ISONG was also concerned about genetic tests being marketed to consumers outside of the patient-health provider relationship (i.e., over the Internet). Other potentially dangerous areas of inappropriate marketing related to testing to identify an individual's rate of metabolism of drugs and testing for ethnic backgrounds.

Dr. Ferreira-Gonzalez thanked Ms. Goldberg and introduced Mr. Patrick Terry.

**Patrick Terry**
**Coalition for 21st Century Medicine**

Mr. Terry stated that he was one of the co-founders of Genomic Health, which developed OncoType DX, an IVDMIA. He was also one of the founding members of the Coalition for 21st Century Medicine, a group that self-organized around the issue of oversight and regulation. It includes industry groups, venture capitalists, academic groups, and disease-specific patient organizations, and attempts to balance oversight and regulation with access and innovation.

He proposed a regulatory framework that the 21st Century Medicine Coalition believed offered specific and detailed approaches for IVDMIAs and multiplexed ASRs, with defined roles for CLIA and FDA and predictable pathways and expectations for test developers, industry, and the investment community. The framework was based on the following concepts: the importance of advanced diagnostics and their continued development, the importance of reimbursement, the rationale for a revised regulatory framework, and detailed regulatory and subregulatory approaches for HHS, FDA, and CMS. The focus was a risk-based approach that included mandatory premarket and postmarket requirements. The proposed registry would be mandatory. Mr. Terry stated that the Coalition was willing to share the framework document with the Oversight Task Force.

Dr. Ferreira-Gonzalez thanked Dr. Terry and closed the session.

**Next Steps and Concluding Remarks**
**Reed Tuckson**

Dr. Tuckson reviewed the accomplishments achieved at the meeting, stating that SACGHS approved the final recommendations in the Pharmacogenomics Report and the report’s content. The Committee also decided to form a Genetics Education and Training Task Force and agreed on several issues to be included in its charge. These included questions about qualifications for providing genetic services, how to regulate and oversee these qualifications, who should receive reimbursement, and the advancement and integration of decision support tools. Dr. Burns McGrath was appointed as Chair of the Task Force. Other Task Force members include Dr. Telfair, Ms. Aspinall, Ms. Au, Dr. Williams, and Dr. Wise. Dr. Tuckson asked the new Task Force to develop a charge for approval at the next SACGHS meeting.

Dr. Tuckson thanked the Committee and adjourned the meeting.

We certify that, to the best of our knowledge, the foregoing meeting minutes of the Secretary's Advisory Committee on Genetics, Health, and Society are accurate and correct.

Reed Tuckson, M.D.
SACGHS Chair

Sarah Carr
SACGHS Executive Secretary